Intensive Care Management of Stroke Patients

J. W. Norris, M.D., MRCP, FRCP(C), and V. C. Hachinski, M.D., FRCP(C)*

SUMMARY Two hundred eighty patients were admitted to an intensive care stroke unit over a one-year period. Subsequent investigation indicated that only 199 of these patients actually had cerebral ischemic or hemorrhagic lesions, 10 had other cerebrovascular lesions, and the remaining 71 patients had unrelated diseases, predominantly seizures. Detailed analysis of 103 stroke patients revealed an overall incidence of 59% hypertension, and 72% had hypertensive, ischemic or valvular heart disease. Fifty percent of the patients had various cardiac arrhythmias, some of which were responsible for the acute cerebrovascular lesion.

Fourteen patients died during the acute phase, 11 from apparently irreversible cerebral swelling, mainly due to cerebral hemorrhage. Secondary complications such as pneumonia, pulmonary embolism, pressure sores and urinary infection were almost nonexistent, but beneficial effects on the primary cerebral lesions were more difficult to demonstrate.

Introduction

THERE HAS BEEN an increasing tendency in recent years to institute intensive care units in virtually every specialty dealing with acutely ill patients. The concept of a stroke intensive care unit or "neurovascular care unit" (NCU) has been in existence for at least ten years; however, there still is conflict of opinion regarding the advantage. This also has been the case with "coronary care units," although there is increasing evidence that they play a valuable role in the management of acute cardiovascular disorders.

However, in view of the large numbers of stroke patients (many of them critically ill) admitted directly to the neurology ward of this hospital, it seemed desirable to institute a unit for the intensive care of stroke patients in the acute phase of their illness and to concentrate facilities and personnel for optimal care.

The data accumulated over the past year in which the unit has been functioning seem of sufficient interest to warrant this preliminary report.

The MacLachlan Stroke Unit

In January, 1975, five intensive care "stroke" beds became operational with continuous neurological nursing care using personnel also trained in cardiac monitoring. Continuous observation of vital signs, ECG and, in some cases, EEG also was routine. Stroke cases were admitted predominantly from the emergency department and the event had to have occurred within 48 hours. The great majority were admitted within ten hours of their stroke. In view of the imminent danger of a catastrophic completed stroke occurring in patients with transient ischemic attacks, these patients were also included. There were no age limits.

As soon as possible after admission, all patients had a skull x-ray, sometimes echoencephalogram, EEG, brain scan, serial ECG, and cardiac enzymes over three consecutive days and a lumbar puncture (unless contraindicated). Special procedures, e.g., carotid angiography, sometimes including cerebral blood flow studies, were performed in a few cases. Many patients needed a cardiological opinion shortly after admission, and all patients were seen by a staff cardiologist during a weekly cardiological ward round. Urinary catheters were not inserted routinely, patients were turned every two hours and rehabilitation started on the day of admission unless contraindicated. Patients were discharged from the unit to the neurology ward when their general and neurological conditions became stable, and continuous vital sign monitoring was no longer necessary. Continuing patient care was the responsibility of the neurological interns and residents, and overall clinical responsibility was taken by two staff neurologists who alternated overall responsibility for the unit in two-month periods.

Results

Population Structure

A total of 280 patients was admitted within the first year, consisting of 209 patients in whom the diagnosis of stroke was confirmed by subsequent investigation. In 71 patients, however, it was apparent shortly after admission or during subsequent investigation that the diagnosis of stroke was incorrect. This "non-stroke" group was composed of postseizure states (34%), acute confusional states, Meniere's disease, senile dementia, etc. One hundred ninety-nine patients were found to have "strokes" in the normal sense of the term, i.e., transient or permanent neurological deficit due to ischemia or hemorrhage of the brain parenchyma.

The majority of the stroke patients had cerebral ischemic lesions (table 1), predominantly completed strokes due to cerebral infarction.

The ratio of the brain stem events to hemispheric events is probably in proportion to the relative ratio of the anatomical compartmental weights except for brain stem hemorrhages where sudden death probably precluded survival long enough for hospitalization. The ratio of hemorrhagic to ischemic events is about 1 in 10.

The age:sex ratio indicates (table 2) that males predominate slightly and are significantly younger.

The average duration of stay in the unit was 5.3 days for stroke patients and 3.1 days for non-stroke patients.

Clinical Observation

Details of a standardized semiquantitative assessment of functional deficit ("stroke score") in stroke patients have been described previously and this was used to measure fluctuations in the course of the illness (figs. 1 and 2). The critical first week in the infarction group probably reflects the patients different stages in the evolution (fig. 3). The patients had various cardiac arrhythmias, some of which were responsible for the acute cerebrovascular lesion.
TABLE 1  **Type and Site of Lesion in Patients With Cerebral Hemorrhage or Ischemia**

<table>
<thead>
<tr>
<th>Type</th>
<th>Cerebral hemisphere</th>
<th>Brain stem</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarction</td>
<td>124</td>
<td>30</td>
<td>154</td>
</tr>
<tr>
<td>TIA*</td>
<td>21</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>14</td>
<td>3†</td>
<td>17</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>154</strong></td>
<td><strong>40</strong></td>
<td><strong>199</strong></td>
</tr>
</tbody>
</table>

*Transient ischemic attack.
†All cerebellar hemorrhages.

essentially the effect of cerebral edema, although there are many other influencing factors.

Routine technetium isotope brain flow and scan on admission have been found very helpful in deciding on underlying structural lesions such as the occasional cerebral tumor or subdural hematoma which initially presents as a stroke syndrome. Using the criteria of either multiple hot spots scattered over the affected hemisphere or the phenomenon of the "hot stroke," a further scan after 10 to 14 days has indicated the high proportion of embolic strokes which may have been otherwise undetected. Such findings often coincide with a slightly hemorrhagic or xanthochromic fluid on lumbar puncture in these patients as well as stepwise or stuttering progression in the stroke scores.

The use of computerized axial tomography (CT) has considerably enhanced the diagnostic accuracy in stroke patients. Only one of the three cerebellar hemorrhage patients in this series was correctly diagnosed prior to CT examination, although this lesion was suspected in all three cases.

**Cardiological Aspects**

Over the past six months, the incidence of hypertension and myocardial disease has been examined in detail in 103 stroke patients. Using sustained blood pressure readings above 160/90 mm Hg as the criterion, 54 (57%) of 95 patients with cerebral ischemic lesions were hypertensive compared to seven (88%) of eight patients with cerebral hemorrhage. These figures are similar to those found by Whisnant et al. Hypertensive, ischemic or rheumatic heart disease was found in 72% of stroke patients compared to 33% in the "non-stroke" group admitted to the unit (table 3). The mean serum cholesterol value in 96 stroke patients was 223 ± 15 mg %, compared to 207 ± 14 mg % in 27 "non-stroke" controls. Serum triglyceride values were 157 ± 12 mg % and 136 ± 12 mg %, respectively. Both values were highly significant (p<0.001) indicating that both cholesterol and triglyceride values were elevated in the stroke group.

Cardiac arrhythmias were found in half of the stroke patients (table 4). In some patients the arrhythmias were believed to be the cause of the ischemic cerebral lesion, but in the majority of patients no direct relationship could be established. The arrhythmias probably reflect simply the influence of diffuse arteriosclerosis. Assuming that patients have acute cerebral ischemia with concurrent atrial fibrillation due to embolization, a surprisingly high causal relationship between cardiac and cerebral ischemic lesions can be seen (table 5). In a few patients, hemodynamic strokes appear to have occurred following the appearance of serious cardiac arrhythmias during or after the stroke, and three patients needed cardiac pacemakers inserted especially when binoxal disease was present. However, sometimes the poor condition of the patient contraindicated this procedure.

**TABLE 2  **Sex and Age Distributions of All Stroke Patients**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number</th>
<th>Mean age ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>109</td>
<td>67.3 ± 8.3</td>
</tr>
<tr>
<td>Women</td>
<td>90</td>
<td>75.2 ± 8.4</td>
</tr>
</tbody>
</table>

**FIGURE 1.** Some examples of the changes in stroke scoring in patients with hemispheric and brain stem hemorrhages. Lumbar puncture (LP) was performed in two patients with unsuspected cerebral hemorrhage causing abrupt but temporary deterioration. + = patient died.

**FIGURE 2.** Some examples of stroke score changes in hemispheric and brain stem infarcts.
Table 3. Incidence of Cardiac Disease and Hypertension in Stroke Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>No cardiac disease</th>
<th>Cardiac disease*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>22 (67%)</td>
<td>31</td>
<td>103</td>
</tr>
<tr>
<td>Controls</td>
<td>22 (67%)</td>
<td>5</td>
<td>33</td>
</tr>
</tbody>
</table>

*Ischemic, hypertensive or rheumatic heart disease.

been seen predominantly in subarachnoid hemorrhage and consist of a prolonged Q-T interval, inverted (often large) T-waves and sometimes S-T segment changes. In two patients with cerebral infarction in this series, similar changes were seen but concurrent, although trivial, serum cardiac enzyme changes favored a diagnosis of subendocardial myocardial infarction. The clinical picture and brain scan in both these patients suggested cerebral embolism, including xanthochromic or bloody CSF, so that the most likely explanation appeared to be mural embolism from tiny areas of endocardial thrombosis. However, the possibility that the ECG changes were consequent upon the cerebral lesion cannot be excluded.

Disturbances of Sleep Rhythm

Apart from the usual value of the EEG in localizing the lesion and deciding upon concurrent epileptogenic features, the value of all-night EEG recordings in stroke patients was investigated. Sleep may be disturbed in any patient admitted to an intensive care unit but, in addition to this commonly observed stress response, there are other changes. These appear to depend partly on whether the lesion is located in the hemisphere or brain stem but also seem to be related to severity. Patients with severely disturbed sleep patterns tend to have significant residual disability compared to those with a similar clinical state but normal sleep records. These results, however, are preliminary and we do not have sufficient numbers to be more specific.

Mortality

Fourteen stroke patients died in the unit over a one-year period, predominantly those with hemispheric cerebral hemorrhage (table 6), the most common cause being brain stem compression subsequent to rostrocaudal herniation of cerebellar tonsils from raised intracranial pressure ("coning").

In four patients combined EEG and ECG tracings were obtained terminally during coning. These indicated progressive slowing and flattening of the EEG tracing followed by progressive sinus bradycardia. Thereafter, some degree of nodal escape ensued with various arrhythmias occurring, this being followed by increasing periods of cardiac arrest up to the final cardiac standstill.

Table 4. Incidence of Cardiac Arrhythmias in Stroke

<table>
<thead>
<tr>
<th>Group</th>
<th>SVPB</th>
<th>VVP</th>
<th>PAF</th>
<th>AF</th>
<th>Other*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>5</td>
<td>23</td>
<td>5</td>
<td>12</td>
<td>7</td>
<td>52 (50%)</td>
</tr>
<tr>
<td>Control</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>6 (18%)</td>
</tr>
</tbody>
</table>

*Binodal disease (2), idioventricular rhythm (1), supraventricular or ventricular tachycardia (4).

Discussion

The evaluation of any new therapeutic measures in stroke, particularly in large patient populations, is hindered by the lack of the universally agreed definition of cerebrovascular disease. Stroke syndromes may vary in description from such meaningless terms as "CVA" to definitions encompassing subarachnoid hemorrhage, subdural hematoma and even cerebral tumor. This failure of any meaningful definition of stroke has bedeviled the attempts of epidemiologists to arrive at any conclusions regarding morbidity or mortality.

It is not likely, nor desirable in many cases, that this process could be reversed since it represents a terminal neurogenic cardiac arrhythmia resulting apparently from progressive vagal stimulation. However, more information regarding this process might be of value in treating those patients whose brain damage is minimal or reversible.

The 7% mortality rate in this initial period (all patients died within the first four days) compares favorably with that reported elsewhere, e.g., 47% in the first month.

Table 5. Relationship of Cardiac Lesion to Stroke in Those Patients With Concurrent Myocardial Disease

<table>
<thead>
<tr>
<th>Relationship</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>None apparent</td>
<td>51</td>
<td>69</td>
</tr>
<tr>
<td>Presumed embolic</td>
<td>20</td>
<td>27</td>
</tr>
<tr>
<td>Associated atrial fibrillation (17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mural emboli (2)</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Prolapsed mitral valve (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binodal disease (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal ventricular tachycardia (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>100</td>
</tr>
</tbody>
</table>

Stroke units vary from small groups of intensive care beds supervised by neurologists (as in our unit) to similar groups primarily under the care of internists or other specialists or to units devoted entirely to rehabilitation when the acute phase of the illness is over. Since the main incidence of mortality occurs in the first few weeks following stroke, and given the wide spectrum of possible diagnoses and the difference between stroke units, comparison of mortality or morbidity between different units is extremely difficult.

Larger multicenter surveys comparing results in stroke care or contrasting the outcome of stroke cases between community and university hospitals indicate a reduction in complications when special care is given to these patients. These surveys are less optimistic, however, about the outcome of the stroke lesion itself.

Table 6. Cause of Death in Patients Dying in the Stroke Unit in One Year

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>No.</th>
<th>Type of stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coning</td>
<td>11</td>
<td>Hemispheric hemorrhages (6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemispheric infarct (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cerebellar infarct (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cerebellar hemorrhage (1)</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>2</td>
<td>Hemispheric hemorrhage (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brain stem infarct (1)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>1</td>
<td>Hemispheric infarct (1)</td>
</tr>
</tbody>
</table>
In a stroke unit very similar to ours, Kennedy et al.1 stated that the maximal therapeutic benefit to be derived was in the subacute phase of the illness where the risk of development of a major complication was considerably lower. They noted no significant difference in death rate in the early stages in the stroke unit compared to that found in the community hospitals. From this viewpoint, such a center, therefore, could not be equated with acute coronary care units where treatment of cardiac arrhythmias in the initial days following the acute lesion is a major factor enhancing survival.

We were impressed by the sharp decline in complications commonly seen in stroke patients, especially deep venous thrombosis, pneumonia, pressure sores and urinary tract infection. The 14 patient deaths, however, do warrant further scrutiny since they may indicate a common denominator in morbidity. Eleven patients died from brain stem compression due to raised intracranial pressure. In six of these, there was extensive brain tissue destruction and it was probable that even if the pathological process could have been reversed, the ensuing quality of life would have been poor. In the remaining five patients, these strictures do not apply and we are now considering methods of reversing this process to allow a timely and acute reduction of raised intracranial pressure. The terminal process was commonly a cardiac arrhythmia, apparently the result of vagal stimulation to the point of nodal escape, and subsequent arrhythmias. Possibly, this terminal effect could be arrested by drugs long enough to allow acute surgical intervention in selected cases similar to the reversal of the ECG changes seen in subarachnoid hemorrhage.16

In any case, those deaths in the first week following the stroke clearly represent overwhelming cerebral catastrophes which may prove difficult or impossible to reduce, the raised intracranial pressure resulting from a mixture of apparently irreversible cerebral edema, necrotic brain and often extravasated blood. The effect of intensive care, therefore, may have minimal impact on death from the primary lesion in the early phase. If intensive care can be shown to reduce mortality and morbidity from complications in the subacute phase, it nevertheless would have a strong reason for implementation not only for humanitarian reasons but also on a cost-benefit basis.

The high incidence of cardiac disease in stroke patients is well established and our results are similar to those previously reported from other intensive care stroke units.17 The most striking correlation, hypertension, may be a causal factor or simply an epiphenomenon indicating generalized arterial disease.

The large number of cardiac arrhythmias in these patients is of uncertain significance. Probably most of the arrhythmias seen play little or no part in the pathogenesis of the stroke lesion and anti-arrhythmic treatment was only occasionally required. Conversely, establishing a cause-and-effect relationship between arrhythmias serious enough to reduce cerebral perfusion is difficult and this mechanism may account for more cerebral ischemic lesions than we have been able to document. There is evidence that cardiac arrhythmia may account for the sudden death or unconsciousness seen in subarachnoid hemorrhage,18 and similar mechanisms may exist in other stroke syndromes.

The only effective way of demonstrating a beneficial effect in the stroke intensive care unit (stroke ICU) is to compare the results prospectively with a similar group of patients treated in a general or community hospital setting. Unfortunately, such a concept is extremely difficult to put into practice. If patients are allocated randomly either to the stroke ICU or to the general neurology ward, management will not be comparable to other hospitals because medical, nursing and rehabilitation personnel will bring to the ward patients expertise acquired in the unit and not available in other hospitals. Comparisons for the control group in another hospital would be invalid unless grounds for common diagnosis of stroke could be ascertained. This could imply an objective sifting through the other hospital's records by a stroke ICU neurologist who would reject cases failing to conform to stroke ICU criteria, thus skewing the figures. Alternatively, lending an "adviser" to a medical unit in another hospital, even if it were found acceptable, would effectively change the diagnostic definition closer to that of the stroke ICU, thus biasing the results. The only alternative would be to match the ICU group with those in a neurology ward similar to this hospital where all stroke patients are admitted to the neurology ward, but no such group exists in this area.

Indirect benefits of the unit, however, are easier to demonstrate and include the accumulation of basic data in a group of stroke patients with accurately delineated lesions and also the introduction of newer diagnostic techniques and the performance of therapeutic trials. The unit constitutes an ideal method of education in the problem of stroke management for all levels of medical and nursing personnel, as well as acting as a catalyst in the generation of new ideas and concepts in all aspects of stroke clinicopathology.

Acknowledgments

We would like to thank all members of the Neurosciences Department at Sunnybrook Medical Centre, including rehabilitation, nursing and medical personnel, for their cooperation in this study. This report represents documentation which was possible only because of the combined teamwork of all involved in the MacLachlan Stroke Unit.

Mr. Graham MacLachlan, himself a victim of stroke, made this Unit possible by his untiring work in organizing and collecting funds from many sources, since the Unit was built entirely on private donations. We would also like to thank the many generous donors involved in setting up the Unit.

In addition, we would like to thank Dr. Hugh Barber, Sunnybrook Medical Centre, who supervised much of the administration of the Unit at its inception, and Dr. J. G. Edmeads, Head of the Division of Neurosciences, Sunnybrook Medical Centre, for his cooperation, help and advice at all stages of its development.

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Dexamethasone and DMSO in Experimental Transorbital Cerebral Infarction
J. C. DE LA TORRE, SC.D., AND J. W. SURGEON, B.A.

SUMMARY Twenty rhesus monkeys were used to evaluate the effects of dexamethasone and dimethyl sulfoxide (DMSO) following experimental occlusion of the middle cerebral artery (MCA) for 17 hours. Animals were initially treated after four hours while the MCA remained occluded and a series of tests was used to evaluate the neurological and cerebral status of each monkey for seven days. The results show that the gross, microscopic and angiographical picture of dexamethasone and no-treatment controls was practically identical. In contrast, DMSO-treated monkeys showed significant protection from the severe neurological deficits seen in the other groups. It is concluded that DMSO has a positive effect in reducing the neurological deficits seen in this model and may be potentially useful in clinical embolic stroke.

WITH MORE THAN 214,000* deaths every year, stroke is the second most important cause of death by disease next to coronary heart disorders. Its annual cost in management for the several million persons disabled every year is estimated at more than four billion dollars in the U.S.* The need to investigate the pathophysiology in a search for potential therapy of this disorder is obviously imperative. The data for coronary heart disorders. It's annual cost in management for the second most important cause of death by disease next to cerebral infarction, and several investigations have examined the relative efficacy of potentially useful approaches. It is fundamental. Although there are some extrapolative limitations in the experimental animal model and the human cerebral infarct, the gross neurological signs and histological damage observed are, in general, quite similar in both species.

Investigations have shown that experimental cerebral infarction may be adequately induced in animals by occluding the middle cerebral artery (MCA) near its bifurcation from the supraclinoid portion of the internal carotid artery using a small aneurysm clip.1•

The transorbital approach (fig. 1) to the MCA offers several advantages over retro-orbital craniectomy: (a) no manipulation of the MCA or retraction of the brain is necessary, thus avoiding vasospasm or cortical tissue damage due to surgical procedure, and (b) surgical decompression is avoided if pathological swelling follows occlusion. The transorbital approach has been used with the same relative results in the squirrel monkey,1 in cats2• and, in the present report, in rhesus monkeys.

Although corticosteroids are often used in clinical and experimental embolic stroke, this therapeutic approach has been questioned in respect to its possible benefits in patients and animals. There is, therefore, an obvious need for a therapy that will neutralize or reduce the devastating effects from the severe neurological deficits seen in the other groups. It is concluded that DMSO has a positive effect in reducing the neurological deficits seen in this model and may be potentially useful in clinical embolic stroke.

*1973 Vital statistics data.

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Methods

Twenty male and female rhesus monkeys (Macaca mulatta) weighing 5 to 7 kg were used. The animals were divided into four groups as follows: (1) shams (N = 2): surgery, exposure and freeing of the MCA from arachnoid but no clipping; (2) controls (N = 8): clipping, 5 ml per kilogram physiological saline; (3) dimethyl sulfoxide (N = 5): 2.5 gm per kilogram in a 50% solution with saline; (4) dexamethasone (N = 5): 3 mg per kilogram in saline, first two doses intravenously and intramuscularly thereafter.

Treatments were given intravenously (except supporting doses of dexamethasone) in adjusted final fluid volumes according to body weight. All animals unable to drink water were kept hydrated by daily intravenous saline fluid replacement.

Respiration and blood pressure were monitored by pressure transducers connected to a Beckman Dynograph
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