Acute stroke treatment in UK hospitals: the Stroke Association survey of consultant opinion

ABSTRACT—The aim of the Stroke Association survey was to document United Kingdom consultant opinion of the immediate treatment for patients with acute stroke. A national postal survey of all UK hospital consultant general physicians, geriatricians and neurologists was carried out in 1992/3. We identified 1,953 consultants who routinely cared for patients with acute stroke; 39% of them regularly used aspirin for patients with acute stroke and 10% used low-dose subcutaneous heparin. Other treatments were rarely used. There was much uncertainty about the effectiveness of all currently available acute stroke treatments; 73% of physicians were prepared to start aspirin before a CT scan, but a much smaller proportion would start heparin therapy without one. Twenty-seven percent of consultants would actively treat hypertension in the initial 24 hours after stroke. Routine aspirin for secondary prevention after ischaemic stroke was widely accepted, but blood cholesterol lowering by drugs was not. In conclusion, aspirin and heparin alone are the only routinely used treatments for the immediate treatment of acute stroke; other treatments are used sparingly or not at all. The great uncertainty about the value of all available acute stroke treatments should encourage participation in randomised controlled trials.

In the United Kingdom, patients admitted to hospital with acute stroke are cared for by consultants working in a variety of hospital specialties, and the delivery of well organised stroke services is patchy and haphazard [1,2], despite the recommendations published by the Royal College of Physicians in 1989 [3]. Information on immediate treatment of patients with acute stroke is scanty, but important for purchasers and providers of acute stroke care and for researchers who are planning large scale randomised controlled trials and assessing the impact of previous stroke research.

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The aims of this survey were to:

- document the immediate medical treatments used for patients with acute stroke in the United Kingdom;
- establish whether UK consultant physicians, geriatricians and neurologists are 'certain' or 'uncertain' of the balance of risks and benefits of various treatments currently available, including the place of blood pressure reduction in the acute phase of stroke;
- investigate whether or not consultants are prepared to start antithrombotic therapy before a computerised tomographic scan has excluded primary intracerebral haemorrhage;
- establish which measures consultants believe to be effective for long-term secondary prevention of stroke among survivors of ischaemic stroke.

Methods

The survey methodology had been published previously [1]. In brief, the names, hospital addresses and specialties of UK hospital consultants were obtained from a commercially available database (Longman Group UK Limited). We selected the physicians who were likely to care for patients with acute stroke, namely those with cardiology, clinical pharmacology and therapeutics, endocrinology, gastroenterology, general medicine, geriatric medicine, infectious diseases, nephrology, neurology, pharmacology and thoracic medicine as their stated specialty. We sent a postal questionnaire to the identified consultants with a covering letter from one of us (JM). Non-responders were sent a further survey form with another covering letter. Only two reminders were sent. Once all replies had been entered on computer, the data file containing personal identifiers was deleted, thus rendering questionnaire responses anonymous for the purposes of analysis. Consultants were asked what treatments they routinely used for patients with acute stroke; how effective they believed such treatments to be; whether they started aspirin, heparin or thrombolytic therapy before or after computerised tomographic scanning; when they treated hypertension in the acute phase of stroke; and how effective they believed routine secondary prevention to be. The questionnaire also covered a range of topics including the provision of hospital stroke services, reported elsewhere [1].

For the purposes of the survey, stroke was defined as 'a sudden onset of focal and at times global (applied to patients in deep coma) neurological deficit with

symptoms lasting more than 24 hours, with a presumed vascular cause and excluding subarachnoid haemorrhage'. Acute stroke was defined as 'onset of symptoms within the previous 7 days'. These definitions were printed on the first page of the questionnaire. The questionnaire replies were coded and entered into a dBase IV database programme (Borland International). The data were analysed using the dBase IV programme and SPSSPC statistics package.

Results

Questionnaires were sent to the 3,478 consultant physicians identified as potentially looking after patients with acute stroke. Replies were received from 2,923 (84%) between December 1992 and October 1993 (after two reminders) and 1,953 of them confirmed that they routinely cared for patients with acute stroke. The reported results are based on the replies from these 1,953 physicians. The proportions of replies by hospital specialty were as follows: general medicine 30%; geriatric medicine 29%; gastroenterology 9%; thoracic medicine 7%; cardiology 7%; endocrinology/diabetes 6%; neurology 5%; nephrology 3%; rheumatology 1%; stroke medicine 1%; other specialties 3% [1].

admitted to UK hospitals by these consultants was estimated to be 107,500 [1]. As a specialty, geriatricians admitted more UK patients than any of the other physicians (40% of the total). The figures for the other specialist groups were: general medicine 29%; gastroenterology 7%; thoracic medicine 6%; endocrinology/diabetes 6%; cardiology 5%; neurology 3%; nephrology 2%; rheumatology 1%; stroke medicine 1%; others 1% [1].

Medical treatments started within 48 hours of onset of symptoms of stroke

The reported use of specific medical treatments for patients with acute stroke is shown in Table 1. Table 2 summarises the clinicians' opinions on the effectiveness of each treatment.

Use of CT scanning before starting aspirin, heparin or thrombolytic therapy

The consultants were asked: 'In practice, do you delay the start of treatment until a CT scan result is known for any of the following treatments for the acute phase of stroke?'. The replies are summarised in Table 3.

Table 1. Replies to the question: 'In the immediate treatment (ie started within the first 48 hours of onset of symptoms) of patients in the acute phase of stroke do you generally use any of the following?'

Treatment	Routinely for most patients		Sometimes for particular patients		Only as part of a randomised trial		Rarely or never		Other	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Antihaemostatic treatments										
Aspirin	753	(39)	767	(39)	51	(3)	339	(17)	43	(2)
Low-dose s.c. heparin[a]	186	(10)	675	(35)	46	(2)	942	(48)	104	(5)
Medium dose s.c. heparin[b]	10	(<1)	301	(15)	59	(3)	1425	(73)	158	(8)
Full i.v. heparinisation[c]	3	(<1)	612	(31)	41	(2)	1212	(62)	85	(4)
Thrombolytic therapy[d]	0	(0)	17	(1)	33	(2)	1816	(93)	87	(4)
Defibrination[e]	0	(0)	4	(<1)	1	(<1)	1857	(95)	91	(5)
Other treatments										
Haemodilution	4	(<1)	86	(4)	1	(<1)	1772	(91)	90	(5)
Dextran (i.v.)	0	(0)	56	(3)	4	(<1)	1801	(92)	92	(5)
Naftidrofuryl (praxilene)	17	(1)	120	(6)	22	(1)	1709	(88)	85	(4)
Gangliosides	0	(0)	2	(<1)	3	(<1)	1843	(94)	105	(5)
Calcium antagonists	7	(<1)	599	(31)	38	(2)	1231	(63)	78	(4)
Mannitol (i.v.)	1	(<1)	218	(11)	3	(<1)	1636	(84)	95	(5)
Glycerol (i.v.)	4	(<1)	37	(2)	3	(<1)	1807	(93)	102	(5)
High dose corticosteroids[f]	5	(<1)	681	(35)	3	(<1)	1187	(61)	77	(4)

[a] 5,000 units twice or three times a day. [b] About 12,500 units twice a day or greater. [c] Full adjusted dose intravenous heparin. [d] eg streptokinase. [e] i.v. ancrod. [f] eg dexamethasone.

The total number of patients with acute stroke

Treatment of hypertension during the acute phase of stroke

Table 2. Responses to the following: 'For patients with acute ischaemic stroke (cerebral infarction) please indicate how effective you believe the following treatments to be in the acute phase (starting within 48 hours of onset)'

Treatment	Definitely beneficial		Definitely harmful		Uncertain effect		Other	
	n	(%)	n	(%)	n	(%)	n	(%)
Antihaemostatic treatments								
Aspirin	586	(30)	17	(1)	1309	(67)	41	(2)
Low dose s.c. heparin[a]	261	(13)	30	(2)	1581	(81)	81	(4)
Medium dose s.c. heparin[b]	61	(3)	120	(6)	1678	(86)	94	(5)
Full i.v. heparinisation[c]	118	(6)	275	(14)	1482	(76)	78	(4)
Thrombolytic therapy[d]	37	(2)	272	(14)	1549	(79)	95	(5)
Other treatments								
Dextran (i.v.)	15	(1)	43	(2)	1793	(92)	102	(5)
Naftidrofuryl (praxilene)	37	(2)	14	(1)	1816	(93)	86	(4)
Calcium antagonists	137	(7)	27	(1)	1704	(87)	85	(4)
Mannitol (i.v.)	30	(2)	48	(3)	1771	(91)	104	(5)
Glycerol (i.v.)	24	(1)	37	(2)	1791	(92)	101	(5)
High dose corticosteroids[e]	122	(6)	144	(7)	1598	(82)	89	(5)

[a] 5,000 units twice or three times a day. [b] About 12,500 units twice a day or greater. [c] Full adjusted dose intravenous heparin. [d] eg streptokinase. [e] eg dexamethasone.

In response to the question: 'How long would you delay before starting treatment for hypertension in a patient with acute stroke (in the absence of an accelerated phase)?' 114 (6%) would not delay starting treatment, 409 (21%) would wait a few hours, 1,132 (58%) would wait a few days, 261 (13%) would wait a few weeks, and there were 37 (2%) 'other' replies.

Long-term secondary prevention

Long-term treatment with aspirin was believed by 1,636 consultants (84%) to be an effective secondary preventive measure after acute ischaemic stroke, 2 (<1%) thought such treatment harmful, 289 (15%) were uncertain of the effect, and there were 26 (1%) other responses. Only 269 (14%) believed that reducing the level of blood cholesterol with drugs was beneficial after acute ischaemic stroke while 1,600 (82%) were uncertain of its effect, 27 (1%) believed such treatment harmful, and there were 57 (3%) other responses.

Discussion

The Stroke Association survey is the first comprehensive survey of the treatment of patients admitted to hospital with acute stroke in the UK. Research based on questionnaires is prone to several sources of error. Low response rates may result in a biased sample, respondents may answer questions to try to please the researchers, or replies made in good faith about, for example, the consultants' usual clinical practice may be less accurate than an audit of their actual practice [4]. We tried to reduce these errors in several different ways. The overall response of 84% indicates that any non-response bias was likely to be small. Every consultant received a personal letter from one of us (JM), and these letters were sent under the auspices of the UK Stroke Association. We hoped that this would encourage clinicians to provide a less biased report than if the questionnaires had been sent by a purchaser or provider of health care. The results of our survey have indicated that nearly 2,000 physicians currently admit patients with acute stroke, so a formal audit of such a large and diverse group of physicians would be prohibitively expensive. In the absence of a formal audit, a questionnaire such as ours is a more practical way of collecting such data.

Treatments routinely used within 48 hours of stroke

Aspirin and low-dose subcutaneous (s.c.) heparin were the only commonly reported treatments routinely used by consultants for the immediate treatment of patients with acute stroke (aspirin by 39%, heparin by 10%). Other treatments were used more selectively (high dose corticosteroids, i.v. heparin, medium dose s.c. heparin, calcium antagonists, mannitol), and some treatments were rarely used (thrombolytic therapy, defibrination, haemodilution, dextran, naftidrofuryl, gangliosides, glycerol).

Table 3. Responses to the question: 'In practice, do you delay the start of treatment until a CT scan result is known for any of the following treatments for the acute phase of stroke?'

Treatment	Always await CT result		Sometimes start before CT result		Always start before CT result		Do not use this treatment		Other	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Aspirin	392	(20)	1098	(56)	321	(16)	98	(5)	44	(2)
Low dose s.c. heparin[a]	325	(17)	546	(28)	193	(10)	797	(41)	92	(5)
Medium dose s.c. heparin[b]	455	(23)	161	(8)	26	(1)	1193	(61)	118	(6)
Full i.v. heparinisation[c]	992	(51)	90	(5)	25	(1)	772	(40)	74	(4)
Thrombolytic therapy[d]	158	(8)	4	(<1)	12	(1)	1680	(86)	99	(5)

[a] 5,000 units twice or three times a day. [b] About 12,500 units twice a day or greater. [c] Full adjusted dose intravenous heparin. [d] Eg streptokinase.

Antithrombotic therapy

Our results indicate that antithrombotic therapy is widely used in the UK to treat patients with acute stroke. Similar results were reported in a survey in the Yorkshire region of England [5] where 63% of physicians reported starting aspirin treatment for patients with 'minor stroke' within 48 hours of the onset of symptoms, and 30% for patients with 'major stroke'. Antithrombotic therapy was also reported to be widely used, in a survey of the clinical practice of 247 USA neurologists [6]. In that study, about a quarter of their patients had been treated with heparin, and most with an adjusted full dose intravenous heparin regime, yet a majority of neurologists were uncertain of the benefits of immediate intravenous heparin [6]. A further study from the USA has confirmed these variations in the use of heparin in patients with acute stroke, and the uncertainties about its effectiveness [7].

Although antithrombotic therapy is widely used, there are no reliable data to support this practice [8]. If routine treatment with aspirin or heparin were to cause even a small excess of early fatal or disabling cerebral haemorrhages, many patients might be harmed by current UK clinical practice [8,9]. Conversely, if antithrombotic therapy were beneficial, many patients would have been denied a useful treatment. The International Stroke Trial (IST) is currently evaluating the balance of risks and benefits of immediate aspirin, s.c. heparin, both or neither, in patients with acute ischaemic stroke. The trial aims to recruit up to 20,000 patients and should provide valuable data on the balance of risks and benefits of immediate antithrombotic therapy [8,10].

Other medical treatments routinely used within 48 hours of stroke

Calcium antagonists and high dose corticosteroids are also of unproven benefit for the immediate treatment of stroke [11–15], yet about a third of all consultants use these treatments selectively for particular patients.

The available evidence cannot exclude the possibility that either treatment may be associated with a small to moderate excess of patients dying or having a poor outcome. The rather disappointing results from earlier trials included patients with *all* types of stroke, and it is possible that a moderate benefit for certain subgroups of patients with ischaemic stroke was overlooked [16,17]. Current UK clinical practice indicates that many consultants feel these treatments have something to offer selected patients. Should further trials be established to evaluate calcium antagonists and high dose corticosteroids (and other specific medical treatments) for selected subgroups of patients?

Clinical uncertainty

Many clinical trials are now based on the 'uncertainty principle' [18,19], ie if a physician considers that, for a particular patient, a certain treatment is definitely effective, the treatment should be given; on the other hand, if a treatment is likely to be definitely ineffective it should be avoided. A clinician who is genuinely uncertain whether or not to give the treatment to a particular patient should consider entering the patient in an appropriate randomised controlled trial. Our survey revealed that more than two-thirds of all consultants were 'uncertain' of the value of the current treatments for acute stroke, which suggests that clinical opinion favours randomised controlled trials of medical treatment in acute stroke in UK hospitals.

Antithrombotic and thrombolytic therapy and the timing of CT scanning

Should CT scanning be routinely performed before starting antithrombotic therapy? The risk that a stroke due to primary intracerebral haemorrhage will be exacerbated with aspirin is not known, but about 15% of all first strokes are due to primary intracerebral haemorrhage [20]. Yet nearly three-quarters of consultants are prepared 'sometimes or always' to start aspirin before a CT scan has established the under-

lying pathology of the stroke. It is illogical to use an antithrombotic drug like aspirin in a patient with a primarily haemorrhagic disorder; it is unlikely that the same consultants would treat a patient with a bleeding tooth socket or a bleeding peptic ulcer with aspirin. Only one-fifth reported that they 'always' waited for the result of a CT scan before starting aspirin. In contrast, just over half 'always' waited for the results of a CT scan before starting full anticoagulation with i.v. heparin; this is probably because of a perceived greater risk of cerebral bleeding with heparin. More consultants were prepared to start the lower s.c. doses of heparin before CT scanning (rather than full-dose i.v. heparin), probably owing to a perceived (but unproven) lower haemorrhagic risk. However, failure to perform a CT scan may not be due to a lack of logic, since CT scanning is not readily available to many clinicians [1]. Furthermore, the council of perfection—that no patient should receive aspirin or heparin before a CT scan—may cause net harm. Most strokes are ischaemic, and delaying treatment until after the scan might, by failing to give early treatment to the majority of patients with ischaemic stroke (perhaps with little if any effect on the minority with haemorrhagic stroke), lead to overall net harm. Since CT scanning is still not universally available in UK hospitals [1] and the balance of risk and benefit of starting treatment without it is unclear, this question is being addressed by the IST. (One of the pre-specified hypotheses being tested is that outcome among patients randomised without CT scanning may be materially better or worse than those randomised with it.)

Not surprisingly, given the greater perceived risk of using the treatment in patients with haemorrhagic stroke, most of the 174 consultants who used thrombolytic therapy 'always' waited for the results of CT scanning.

Treatment of hypertension

There is evidence that lowering blood pressure in the acute phase of stroke may be harmful [15], yet over a quarter of physicians would treat hypertension (in the absence of an accelerated phase) within 24 hours of onset of symptoms. On the other hand, there may be benefits from moderate reductions in blood pressure in the weeks and months after surviving a stroke [21]. We believe more research is needed to evaluate the balance of risks and benefits of early blood pressure reduction for patients with acute stroke.

Secondary preventive measures

The results of the first cycle of the Antiplatelet Trialists' (APT) collaborative overview analysis were published in 1988 [22]; we were therefore rather surprised to find that 15% of consultants, in 1993, were still uncertain of the balance of risks and benefits of long-term treatment with aspirin for patients with ischaemic stroke. This 'uncertainty' may have been due, in part, to the debate as to whether women benefited from such treatment—a debate that has only been resolved by the publication of the second cycle of the APT [23]. We hope the convincing nature of these later analyses will persuade those physicians who have doubted the value of routine antiplatelet therapy in long-term secondary prevention to consider such treatment for all their patients who have survived an ischaemic stroke. Delays in the implementation of the results of medical research have been demonstrated in other areas of medicine, for instance the treatment of myocardial infarction [24]. Review articles and textbooks have often been very slow in recommending treatments shown to be effective, and even in ceasing to recommend established treatments later shown to be ineffective or dangerous [24]. In order to improve the quality of the data available to clinicians, the Cochrane Collaboration has been established to organise and disseminate regularly updated systematic reviews of the results of randomised controlled trials. The first set of results published by that group are available on computer disc or CD-ROM (BMJ Publishing Group, London), and eventually these data should be available 'on line' to anyone with a computer and a modem. We hope that initiatives such as the Cochrane Collaboration will provide more reliable data on the balance of risks and benefits of medical treatments (and management strategies) to guide clinicians in their routine clinical practice.

Lowering blood cholesterol by drugs as a secondary preventive measure after ischaemic stroke is controversial; most physicians were uncertain of its effectiveness. This question is now being addressed in the MRC/British Heart Foundation heart protection study [25] (Rory Collins, personal communication), and our survey confirms that this is an important area of uncertainty for UK physicians and neurologists.

Auditing future research

Our survey has established a baseline for measuring the impact of publishing the results of future research into treatment of acute stroke. A 'before and after' study [26] on the impact of the results of the ISIS-2 [27] and GISSI [28] trials on the treatment of patients with acute myocardial infarction demonstrated a dramatic change in clinical practice which was almost certainly an outcome of the trial publications. Future surveys could be compared with our results to monitor changes in clinical practice and assess the impact of the publication of randomised controlled trials.

The future

The uncertainties of the value of treatments for the immediate phase of stroke reflect the paucity of randomised controlled data in this area. The Stroke

Review Group of the Cochrane Collaboration has started to collate the currently available evidence for the completed randomised controlled trials of treatments of acute stroke [29]; the first phase of this review has been published [30]. More important, the Cochrane Collaboration has established a method of systematically reviewing accumulating data and disseminating the results not only electronically but also by publication in established general medical journals. We hope that this will give clinicians routine access to the best available data, and that, where uncertainty exists, they will participate in appropriate randomised controlled trials.

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