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Ischaemic brain damage is still common in fatal non-missile head injury

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SUMMARY A detailed neuropathological examination has been undertaken on a consecutive series of head injuries dying in the Institute of Neurological Sciences, Glasgow, between 1968–72 (151 cases) and 1981–82 (112 cases) in order to determine the frequency and distribution of any ischaemic brain damage. Ischaemic damage was found in the brains of 92% of the 1968–72 cases and in 88% of the 1981–82 cases: there was no statistical difference in the amount of moderately severe and severe ischaemic damage in the two groups, 55% and 54% respectively. There was evidence, however, that an increased number of patients with severe ischaemic brain damage was admitted in 1981–82 as a result of a changed admission policy of the Department of Neurosurgery that resulted in an increased detection of intracranial haematomas. It is concluded that ischaemic brain damage is still common after severe head injury, and it seems likely that it remains an important cause of mortality and morbidity.

It was not until the 1970s that there was full recognition of the frequency and distribution of ischaemic brain damage in fatal non-missile head injury, and that much of this damage could be attributed to a critical reduction in regional blood flow.[1] In the West of Scotland this led to increased attention to the recognition and treatment of hypoxia and hypotension at the scene of the accident, during interhospital transfer,[2] in critical care units and to the detection and relief of cerebral compression from traumatic intracranial haematoma.[3] Regimens of management and organisation of patient care with broadly similar principles have been employed in many other centres.[4–8] The aims of this study were to compare and to contrast the results of the detailed neuropathological analysis of the occurrence of ischaemic brain damage in two groups of fatally head-injured patients treated in the West of Scotland Regional Neurosurgical Unit, the first between 1968 and 1972, and the second between 1981 and 1982.

Materials and methods

During the 15 year period 1968–82, necropsies were undertaken on 635 fatal non-missile head injuries that had been treated in the Department of Neurosurgery in this Institute. There were 497 (78%) males and 138 (22%) females, aged 9 weeks to 89 years (median 36 years) (table 1); the duration of survival ranged from 1 hour to 14 years 3 months (median 2–3 days). The present analysis concerns the 151 (Group 1) cases dying between 1968–1972 and the 112 (Group 2) cases dying between 1981–1982. Every case was subjected to a comprehensive histological analysis. The necropsy rate on fatal head injuries dying in this Institute in 1968 was 68%, and on average 83% for the other years covered in this study. The investigation would not have been possible without the willing cooperation of the forensic pathologists in the West of Scotland who allowed us to fix the brains intact before dissection.

The two groups of fatal cases were drawn from the head injuries occurring in the same geographical area with a population of approximately 2·7 million, but from different total numbers of cases admitted to the Neurosurgical Unit. In the West of Scotland, as in most of the United Kingdom, all head injured patients are taken first to a district general hospital for initial assessment, resuscitation and stabilisa-

Table 1 *Age (yr) and sex*

	Group 1 (n = 151)	*Group 2 (n = 112)*
Minimum age	1	1
Maximum age	86	89
Median age	40	39
Male:female	4·4:1	3·9:1

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Table 2 *Type of injury and survival*

	Group 1 (n = 151)		*Group 2 (n = 112)*		
	n	*Incidence*	*n*	*Incidence*	*'p' value*
RTA	69	(13·8)	66	(33)	
Fall	66	(13·2)	34	(17·5)	< 0·025
Others	16	(3·2)	12	(6)	
< 72 hours	79	(15·8)	73	(36·5)	
> 72 hours	72	(14·4)	39	(19·5)	< 0·05

RTA = road traffic accident

tion. Only a small proportion are subsequently transferred for neurosurgical assessment and treatment. This proportion, and hence the total number of cases transferred per year, increased between the periods 1968–72, and 1981–82.

Hospital statistics were screened to gain data about the total number of head injured patients treated in the Neurosurgical Unit in the two periods being analysed. In 1968, 1969, 1970 and 1972 the total numbers were 295, 256, 193 and 196 respectively (data for 1971 are not available as a result of the Unit moving to a new site). In 1981 and 1982 the number of admissions due to acute head injury were 637 and 694 respectively. The increase in the average admission rate from 235 per year to more than 600 per year reflected the adoption by the neurosurgeons in 1978 of a policy aimed at earlier transfer to their unit of all patients at risk of an intracranial complication. This resulted in an increased detection of intracranial haematoma and an improved outcome in operated cases;[3] there was also an increase in the use of ventilatory treatment which was employed in only 17% of the cases in the 1968–72 group but in 68% of those in the 1981–82 group. Mortality figures for all head injury patients in the two era are not available; in patients judged as severe, by virtue of remaining in coma for more than six hours, 54% died within six months of injury between 1968–72 and 50% in 1981–82. This in part reflected an increase in the number of patients with a head injury that was severe from the outset.[9]

A full necropsy was undertaken in every case and the brains and spinal cords were fixed in 10% formol saline for at least three weeks before dissection. The cerebral hemispheres were cut in a standard fashion[10] in the coronal plane, the cerebellum at right angles to the folia, and the brain stem horizontally. Comprehensive histological studies, including the examination of large celloidin sections of the brain, were carried out on every case. Macroscopic and histological abnormalities were recorded on a series of line diagrams of the cerebral hemispheres, cerebellum and the brain stem. All abnormalities were then transferred to a proforma and the data stored and analysed on the University of Glasgow's mainframe computer.

Table 3 *Lucidity (ability to talk after injury)*

	Group 1 (n = 151)		*Group 2 (n = 112)*		
	n	*Incidence*	*n*	*Incidence*	*'p' value*
Present	58	(11·6)	25	(12·5)	< 0·01
Absent	93		85		

Not known in 2 cases (1981–82)

Table 4 *Skull fracture, contusions, supratentorial haematomas, diffuse axonal injury and brain swelling*

	Group 1 (n = 151)		*Group 2 (n = 112)*		
	n	*Incidence*	*n*	*Incidence*	*'p' value*
Fracture of skull	120	(24)	91	(45·5)	NS
Contusions					
Mean, (SD)		18·67, (13·29)		22·03, (14·99)	< 0·05
Median		17·00		20·00	= 0·048
Supratentorial haematomas	106	(21·2)	92	(46)	< 0·05
Diffuse axonal injury	21	(4·2)	25	(12·5)	NS
Swelling—total	60	(12)	66	(33)	< 0·005
—bilat.	22	(4·4)	27	(13·5)	< 0·05

The severity of ischaemic brain damage was graded. *Severe* comprised those cases in which the lesions were diffuse, multifocal and large within the distributions of arterial territories; *moderate* when the lesions were limited to the arterial boundary zones, singly or in combination with subtotal infarction in the distribution of the cerebral arteries, or if there were 5–10 subcortical lesions; and *mild* if there were five or less small lesions in the brain.

The clinical records of patients were assessed for evidence of a lucid interval, that is, the ability to talk, before deterioration in the conscious level.[11]

Statistical analysis

The data presented in tables 2–10 are for the most part categorical, the exception being the contusion index data in table 4. The statistical analysis of the categorical data has been based on Pearson's chi-square statistic. Note that this test contrasts the *proportions* of cases in the various categories between the two groups. To help in the interpretation of these tests and to identify whether changes in *proportions* could be associated with differential changes in *incidence* of the various outcomes, the per annum incidence rates of the outcome categories are given in parenthesis after the corresponding frequencies. The contusion index data were analysed using the Mann Whitney test since the contusion indices are not normally distributed.

Results

The age and sex distribution at the time of injury are shown in table 1: there were no differences between the

Table 5 *Raised intracranial pressure*

	Group 1 (n = 151)		*Group 2 (n = 112)*		
	n	*Incidence*	*n*	*Incidence*	*'p' value*
Present	131	(26·2)	97	(48·5)	NS
Absent	20		15		

Table 6 *Ischaemic damage in cerebral cortex—diffuse*

	Group 1 (n = 151)		Group 2 (n = 112)		
	n	Incidence	n	Incidence	'p' value
Present	43	(8·8)	47	(23·5)	< 0·05
Absent	108		65		

groups. The type of injury and survival are given in table 2, from which it can be seen that there was a statistically significant higher proportion of falls and a survival equal to or greater than 72 hours in Group 1 than in Group 2, whereas there was a higher incidence of admissions following road traffic accidents (RTAs) in Group 2 than in Group 1. Lucidity is analysed in table 3, from which it can be seen that more cases had been lucid in Group 1 than in Group 2.

The case records were analysed for details of known episodes of clinical hypoxia (systolic blood pressure < 80 mm Hg for at least 15 mins, or a PaO_2 < 50 mm Hg at some time after the injury). No statistically significant differences were found between hypoxia, hypotension, haemorrhage, extracranial fractures or soft tissue injuries in the two groups.

Details of skull fracture, contusions as assessed by the contusion index,[12] supratentorial haematoma, diffuse axonal injury[13] and brain swelling are shown in table 4, from which it can be seen that although there was a higher proportion of all these features in Group 2 than in Group 1, it was only with respect to contusions, supratentorial haematoma and swelling that there was a statistically significant increase in Group 2. Using the criteria of pressure necrosis in one or both parahippocampal gyri as evidence that the intracranial pressure had been high during life,[14] it can be seen from table 5 that there were similar proportions of patients with raised intracranial pressure in the two groups.

The frequency and principal patterns of ischaemic brain damage in the cortex are given in tables 6 and 7, and in subcortical structures in table 8. From table 6 it can be seen that the proportion of cases with diffuse damage in the cortex of the type seen after cardiac arrest or status epilepticus was greater in Group 2 (p < 0·05) than in Group 1, whereas from table 7 it can be seen that ischaemic damage in the arterial boundary zones[15] was proportionally more common in Group 1 than in Group 2. The amount of ischaemic damage in various subcortical structures is shown in table 8; it was higher in Group 2 than in Group 1 although statistically significant differences were limited to the striatum and globus pallidus in Group 1. These findings are summarised in table 9, from which it can be seen that whereas there was a greater proportion of cases with diffuse cortical damage in Group 2 than in Group 1, there was a higher proportion of cases with cortical arterial boundary zone damage in Group 1 than in Group 2. Ischaemic damage was also present in many of the subcortical structures, there being larger numbers of cases with lesions in the basal ganglia in Group 1 than in Group 2. There was no statistical difference in the overall number of cases with ischaemic brain damage in the two groups, and furthermore there were similar proportions of cases having either no ischaemic brain damage or similar amounts with either moderate or severe ischaemic brain damage, even though the incidence of severe ischaemic damage was greater in Group 2 than Group 1. A comparison showing that there was no statistically significant difference in either frequency or severity of ischaemic brain damage between the two groups is given in table 10, with 92% of the 1968–72

Table 7 *Ischaemic damage in cortex—arterial boundary zone*

	Group 1 (n = 151)		Group 2 (n = 112)		
	n	Incidence	n	Incidence	'p' value
Present	38	(7·6)	15	(7·5)	< 0·025
Absent	113		97		

Table 8 *Ischaemic brain damage in other sites*

	Group 1 (n = 151)		Group 2 (n = 112)		
	n	Incidence	n	Incidence	'p' value
Hippocampus	123	(24·5)	90	(45)	NS
Striatum	70	(14)	38	(19)	< 0·05
Globus pallidus	55	(11)	27	(13·5)	< 0·05
Thalamus	86	(17·2)	63	(31·5)	NS
Total cases	137	(27·4)	97	(48·5)	NS

Table 9 *Comparison of ischaemic brain damage (IBD) in the two groups*

	Group 1 (n = 151)		Group 2 (n = 112)		
	n	Incidence	n	Incidence	'p' value
Diffuse	43	(8·6)	47	(23·5)	< 0·05
Arterial boundary zone	38	(7·6)	15	(7·5)	< 0·025
Arterial territory	25	(5)	21	(10·5)	NS
IBD in other sites	137	(27·4)	97	(48·5)	NS

Table 10 *Comparison of ischaemic brain damage—severity*

	Group 1 (n = 151)		*Group 2 (n = 112)*		
	n	*Incidence*	*n*	*Incidence*	*'p' value*
Absent	12	(24)	13	(6·5)	NS
Mild	56	(11·2)	39	(19·5)	NS
Moderate	50	(10)	25	(12·5)	NS
Severe	33	(6·6)	35	(17·5)	NS

cases having some ischaemic brain damage as compared with 88% of the 1981–82 cases. This ischaemic damage was moderate or severe in 55% of cases in Group 1 and 53% in Group 2.

A summary of the principal findings is given in table 11. In Group 1, falls, a survival of > 72 hours, a lucid interval and ischaemic damage in arterial boundary zones of the cortex and in the striatum, the globus pallidus and other deep structures were more common than in Group 2. In Group 2 there was a statistically significant increase in injury due to road traffic accidents, supratentorial haematoma, brain swelling and diffuse ischaemic brain damage.

Discussion

Ischaemic brain damage is common in patients who die after a non-missile head injury and, in our experience, was as common in the early 1980s as in the late 1960s and early 1970s. It seems likely therefore that it remains an important cause of mortality and probably also of morbidity in patients who survive a severe head injury.

It is necessary, in interpreting the findings of this study, to note that they reflect cases drawn from two very different populations. Thus, in the period covering Group 2, there were almost three times more head injuries per year admitted to the Neurosurgical Department than between 1968–72. These included greater numbers of patients with injuries that were severe from the start and who never talked; such patients were transferred more rapidly than in 1968–72. In the earlier time period, patients were observed for longer before transfer, which was usually arranged only after the patient had shown deteriorating consciousness thought to be a result of a compressing intracranial haematoma. The change in policy led to an increased detection of intracranial haematomas and to improved results in operated cases.[3]

Table 11 *Statistical differences between the two Groups*

	Group 1	*Group 2*
RTAs	—	More common
Falls	More common	—
Survival > 72 hrs	More common	—
Lucidity	More common	—
Supratentorial haematoma	—	More common
Brain swelling	—	More common
Ischaemic damage		
(a) in cortex		
—diffuse	—	More common
—arterial boundary zone	More common	—
(b) in other sites		
—striatum	More common	—
—globus pallidus	More common	—
—others	More common	—

Despite these differences, the age, sex distribution and survival were similar in these two groups of fatal cases. In contrast, there was a higher incidence of injuries due to a fall between 1968–72 (Group 1) than between 1981–82 (Group 2), the converse being true for RTAs, and more cases died within 72 hours and fewer had a lucid interval in Group 2 than in Group 1. There was a higher incidence of supratentorial haematomas, diffuse axonal injury and brain swelling in Group 2 than in Group 1, but the proportion of cases with structural evidence of raised intracranial pressure was the same in the two groups. These findings are perhaps rather surprising as it might have been expected that the pattern of damage would have reflected more closely the type of injury. Thus it is reported that there is a higher incidence of fracture of the skull, contusion, intracranial haematoma and raised intracranial pressure after a fall than a RTA.[13] In the present data the reverse was almost true insofar as supratentorial haematoma and brain swelling were more common in Group 2, which contained more cases of RTA than a fall, than in Group 1 in which the opposite was true.

The fact that the proportion of cases with raised intracranial pressure was the same in the two groups might explain why the amount of ischaemic brain damage in Group 1 (92%) was similar to that in Group 2 (88%), as much of the ischaemic damage in fatal head injury is attributable to distortion and internal herniation of the brain in relation to a high intracranial pressure.[16] It is, however, also clear that a considerable amount of the ischaemic damage is due to the changes in cerebral perfusion pressure irrespective of a high intracranial pressure.[17] Raised intracranial pressure and ischaemic brain damage can be produced by many factors and the pattern of ischaemic brain damage is related to mechanisms.[16,17] In view of the differences in type of injury and other findings in the two groups, changes in occurrence of varying patterns of ischaemic brain damage might therefore be expected.

The ischaemic damage in the cerebral cortex took several forms. Between 1968–72 it was most commonly centred on the boundary zones between the major cerebral arterial territories, particularly between the anterior and middle cerebral arteries, and in the majority of cases it was bilateral. Diffuse damage

in the cerebral cortex, on the other hand, was more common between 1981–82 than 1968–72. The proportion of cases in the two groups with ischaemic brain damage within specific arterial territories was similar, probably reflecting the equal proportion of cases with raised intracranial pressure (see table 9).

The pathogenesis of ischaemic brain damage is not yet fully understood, but in the series described by Graham *et al*[1] it was significantly more common in patients who had sustained a known clinical episode of hypoxia (hypoxaemia or hypotension) and/or a high intracranial pressure during life. The high incidence of damage to the cerebral cortex in the arterial boundary zones in the 1968–72 series suggested that perfusion failure due to a transient reduction in cerebral blood flow was at least a contributing factor. The institution of measures to maintain adequate cerebral perfusion (including maintenance of adequate airway and blood gases, and the prompt correction of hypotension by replacement of blood volume) should therefore be reflected in a reduced incidence of infarction within the arterial boundary zones. Indeed this was found to be the case in the 1981–82 (Group 2) series of cases.

Diffuse ischaemic brain damage, on the other hand, is usually a consequence of either cardiorespiratory arrest or status epilepticus. It is interesting to note that the incidence of this type of ischaemic damage was higher between 1981–82 than in 1968–72. This perhaps is rather surprising as it would have been expected that modern resuscitative measures would have at least to some extent reduced this type of ischaemic brain damage. On the other hand, the events responsible may occur almost immediately after the injury, before first admission to hospital and even before the arrival of any skilled personnel at the scene of the accident. In view of the increase in the number of severely head injured patients who were transferred to the Department of Neurosurgery, it is not surprising that there is an increased incidence of diffuse ischaemic brain damage in those cases dying within the Institute who, prior to the change in admission policy, would have died in accident and emergency departments or in primary surgical wards. It is probably for this reason also that there is no apparent change in the overall severity of ischaemic brain damage between the two groups of cases.

The changes in the pattern of the incidence of the lesions and their proportions reflect the effects of a change in clinical practice, in particular in the policy of the Department of Neurosurgery. Nevertheless, this study has shown that ischaemic brain damage is still common in patients dying from head injury in this Institute. Improvements in the management of head injured patients should still be aimed at avoiding the occurrence of ischaemic brain damage or at minimising its consequences.

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