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Short report

Cerebral infarction does not occur typically at night

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SUMMARY In a hospital-based series of 66 consecutive patients with non-progressive cerebral infarction, the time of onset and the type of infarction on computed tomography were studied retrospectively. Forty-six (78%) patients suffered cerebral infarction between 6 am and 6 pm. Only five patients (8%) had their infarct between midnight and 6 am. Only three patients had a watershed-infarct, and these occurred during the daytime. Our results do not support the belief that atherothrombotic brain infarction is largely determined by haemodynamic factors.

Traditional teaching holds that cerebral infarction occurs more often at night than during the daytime and that symptoms are usually noticed on waking. This, in combination with the fact that blood pressure is lower during the night, fits the notion of cerebral "thrombosis". However, the evidence that cerebral infarction is a nocturnal illness[1 2] is not convincing. In those studies, the diagnosis of cerebral infarction was imprecisely defined, or more importantly, patients with incomplete information have not been taken into account. To shed some new light upon this problem, we have, in a retrospective review of patients recently admitted with cerebral infarction, attempted to retrace the exact time of onset in each patient. In addition, we studied the type of infarction (in the territory of a single artery or between different territories), as this provides some evidence for embolism or haemodynamic factors, respectively.

Patients and methods

Between 1 January 1984 and 1 September 1985, 99 patients were diagnosed as having cerebral infarction. To facilitate comparison with one previous study,[1] we adopted the same criteria for "stroke of acute onset", in that symptoms should have reached their maximum in less than 6 hours and should have remained present for at least 3 weeks. For the same reason, we divided the day into four periods of 6 hours. The time of onset was retrieved from the hospital notes or, if those were uninformative, we interviewed the patient or witnesses.

Thirty-three of the 99 patients were excluded because of clinical regression within 3 weeks (five cases), progression for more than 6 hours (18 cases), concomitant cerebral haemorrhage (three cases), a co-existent tumour (one case), trauma (two cases), migraine (one case) or because cerebral infarction occurred during general anaesthesia (three cases).

CT was performed on admission, with an Ohio Nuclear Delta Scanner or Philips Tomoscan 300/310. If the scan did not show a relevant infarct and the stroke onset had been less than 3 days before, it was repeated approximately 10 days later. Four types of infarcts were distinguished: (1) infarct in the territory of a main arterial trunk (complete or incomplete); (2) lacunar infarct, in the deep regions of the brain or brain stem; (3) watershed infarct, between the cortical territories of the main arterial trunks, or between the territories of the superficial and deep branches of the middle cerebral artery; (4) no lesion visible; these were either patients with the clinical signs of lacunar infarction but with lesions undetected by CT, or patients with severe deficits of less than 48 hours duration in whom CT could not be repeated because of early death from brain swelling and herniation.

In 12 patients the infarct was associated with a possible source of embolism from the heart: atrial fibrillation (five cases), myocardial infarction within the last 6 months (six cases), or valvular heart disease (one case). Blood pressures were the highest recorded measurements in the first 3 hours after admission. The readings had been obtained with an ordinary sphygmomanometer by resident physicians or

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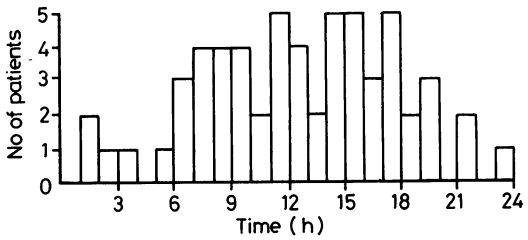

Fig *Time of onset of cerebral infarction, in 59 patients.*

nursing staff. High blood pressure was defined as a diastolic blood pressure of 110 mm Hg or more.

The results of this study were statistically tested by means of the confidence interval for a "normal" binominal division.

Results

The exact time of onset (to the nearest hour) could be retrieved in 59 of the 66 patients (fig). These included five patients who suffered their stroke in bed. Of the remaining seven patients, four slept from some time before midnight until after 6 o'clock before discovering their deficits, and three others were found with an impaired level of consciousness but out of bed. In the 59 patients with a known time of onset, 46 suffered their infarct between 6 am and 6 pm (78%), and five infarcts (8·5%) occurred between midnight and 6 am. The difference between the incidence of infarction during the daytime and that in the evening and night is statistically significant because the 99% confidence interval of daytime infarcts is 65–88%. Even if all seven patients with an unknown time of onset are assigned to the period between 6 pm and 6 am, the proportion of daytime infarcts is 70% (99% confidence interval 57–80%).

Only three patients had watershed infarcts, in one case combined with an infarct in the main territory of the middle cerebral artery. All these three infarcts occurred during the daytime (table).

The time of onset in patients with lacunar infarcts, with (yet) invisible infarcts, with possible embolism from the heart or with hypertension was distributed as in the other patients. Only two patients had a diastolic blood pressure of less than 70 mm Hg; both had a lacunar infarct, during the daytime.

Discussion

The time of onset of cerebral infarction could be reliably determined, except in 10% of the patients who slept until late in the morning or who were alone and could not tell their own story. Consequently, the results would not have been different if the study had been prospective. The results clearly indicate that cerebral infarction occurs mostly between 6 am and 6 pm and not at night. This is contrary to traditional ideas reflected in many textbooks and apparently confirmed by two previous studies that found 41% of infarctions occurring between midnight and 6 am,[1] or 31% between 1 am and 5 am.[2] Our results differ from these studies even if the seven uncertain cases are included in the night group. A possible explanation for the difference is that the previous studies did not take account of patients in whom the exact time was unknown, although these constituted a fair proportion: 20%[1] and 21%.[2] Our findings are in better agreement with the results of three other studies,[3-5] although a strict comparison is not appropriate because the diagnosis of cerebral infarction was imprecisely defined,[3] or included patients with TIAs and regressive strokes,[4] or excluded patients aged over 70 years or patients with an unknown time of onset.[5] If we had included the five patients in whom the clinical deficits regressed within 3 weeks, the results would have been similar, as in only one of them the stroke occurred during the night. In the 18 patients with progressive stroke the symptoms had developed so gradually that it was not possible to determine the hour of onset with any degree of certainty, at least retrospectively.

It should be stressed that this study is hospital-based, but so are the earlier studies. We cannot

Table *Time of onset of cerebral infarction in 66 patients, related to embolic heart disease, blood pressure and type of infarction*

Period (hours)	*All cases*	*Probable embolism from the heart*	*Diastolic blood pressure 110 mm Hg or more*	*Territory of main artery*	*Lacunar*	*Watershed or terminal zone*	*No lesion visible*
0.01– 6.00	5	0	1	2	2	0	1
6.01–12.00	22	2	6	14	4	1	3
12.01–18.00	24	7	9	14*	5	1*	5
18.01–24.00	8	2	0	5	2	1	0
Unknown	7	1	4	4	2	0	1
Total	66	12	20	39	15	3	10

*One patient showed both types of infarction.

exclude the possibility that many patients with "early morning strokes" are referred to geriatric care, and not to hospital. In a recent population-based study in Oxfordshire, however, most strokes occurred during the day (Warlow, personal communication). The classical theory of cerebral "thrombosis" holds that the combination of atherosclerotic disease and a physiological fall in blood pressure during the night causes ischaemia, as the sluggish circulation cannot be compensated by autoregulation. Our finding that most cerebral infarctions occur during the daytime seems to indicate the opposite. Furthermore, the few cerebral infarcts that did develop during the night time were not in watershed areas, which type one would expect in case of a haemodynamic crisis.[8] Even in fatal cases of hypotension (from cardiac arrest) no relation exists between the degree of extracranial atherosclerosis and the occurrence of cerebral infarction,[6] so it is doubtful whether hypotension often plays a role in the pathogenesis of atherothrombotic brain infarction.

Some who found relatively more cerebral infarctions during the day have suggested that temporary hypertension causes cerebral ischaemia, by a breakdown of autoregulation.[3 5 7] In our study, CT showed that most infarcts were in the territory of a single arterial trunk, consistent with embolism.[8] In keeping with this, we found no difference in time of onset and type of infarction between patients with a source of embolism in the heart and other patients, in contrast to previous studies.[9 10] Therefore, the distinction between patients with "cerebral embolism" (from the heart) and "cerebral thrombosis" seems rather arbitrary. This conclusion is supported by the post-mortem studies performed by Lhermitte, who found evidence for artery-to-artery embolism from stenotic or ulcerative lesions of the extracranial arteries.[11]

Explanations accounting for the diurnal variation in the chain of events that link extracranial atherosclerosis and cerebral infarction should probably include factors such as viscosity and platelet aggregability rather than a drop in blood pressure.

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