Holter Monitoring in Patients With Transient and Focal Ischemic Attacks of the Brain

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SUMMARY The results of Holter monitoring in 100 patients with transient and focal cerebral ischemia were studied retrospectively. Atrial fibrillation (AF) was found in five patients compared with two from a group of 100 age and sex-matched control patients. Four of these had a previous history of AF or showed AF on the standard electrocardiogram. Episodic forms of sick sinus syndrome, which have also been related to cerebral embolism, were found in 32 of the TIA patients against 13 of the controls (p < 0.0025). Sick sinus syndrome was of the bradyarrhythmia-tachyarrhythmia type in 14 of the TIA patients and in three of the controls (p < 0.01). The relationship between TIAs and transient sinus node dysfunction could not be explained by concomitant heart disease. It is not yet clear whether the relationship is causal or indirect.

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CARDIAC DYSRHYTHMIAS may cause transient neurological symptoms in two ways: (1) by diminishing cardiac output, which may lead to generalized cerebral symptoms, such as dizziness, syncope, etc., and (2) by predisposing to thrombus formation in the heart, with subsequent embolism and focal cerebral dysfunction. The importance of continuous ECG recording in cerebral infarction in normotensive and hypertensive subjects. J Neurol Sci 24: 243-250, 1975


Appendix

Special Project Ischemic Brain Disease OD2

Participant Units

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on admission. On the other hand, Abdon et al8 stressed that Holter monitoring might be important for the detection of mild and episodic sick sinus syndrome, as this may also be related to cerebral embolism. They found that these transient dysrythmias occurred significantly more frequently in patients with TIAs and unexplained stroke than in a reference population. However, this control group was not matched for age and sex.

The present study undertook a retrospective review of Holter monitoring in 100 patients with transient focal cerebral ischemic attacks, and compared the results with those in an age and sex-matched control population.

Patients and Methods

TIA and Control Population

In the period between January 1980 and May 1983, 172 consecutive patients were admitted to the neurological department of the University Hospital of Rotterdam with a diagnosis of transient and focal attacks of cerebral ischemia, lasting less than 24 hours and
leaving no deficit. Diagnosis was based upon internationally accepted criteria. The patients were independently interviewed by two physicians, who then discussed the history. If they did not agree on the diagnosis, at least one more neurologist was consulted.

In 58 cases, Holter monitoring was not performed. The reasons were technical problems (7 cases), evidence of atrial fibrillation on the initial electrocardiogram (6 cases) and unknown reasons (45 cases), occurring mainly in the period before September 1980 when Holter monitoring was not yet used as a routine investigation in our department. In 14 other patients the period between the neurological symptoms and Holter monitoring exceeded three months, the limit we adopted in this study.

The remaining 100 patients, 74 men and 26 women, ranging in age from 22 to 80 years, with a mean age of 60.9 years, formed the basis of this study. The mean time between recording and neurological symptoms was 15.2 days.

From April 1984 till February 1985, 100 age and sex-matched control patients were selected. These were all in-patients of the University hospitals of Rotterdam and Utrecht and had no previous or present history of focal ischemic brain disease, whether transient or permanent, of peripheral embolism or of treated arrhythmias. Patients who showed physical signs of valvular heart disease or congestive heart failure, and also patients with evidence of recent myocardial infarction on a standard electrocardiogram were excluded. General risk factors for cardiovascular disease such as diabetes mellitus and hypertension were no reason for exclusion. An old (at least one year) myocardial infarction and an enlarged heart on X-ray as a single finding (see table 1) were also accepted.

Ninety-two patients were admitted with neurological disorders not associated with cerebrovascular disease, such as polyneuropathy, spondyloitic myelopathy, cerebral tumor, Parkinson’s disease, lumbar disk disease or multiple sclerosis. None of the patients had neuromuscular disease known to cause cardiomyopathies. The other eight patients were admitted with urological disorders such as nephrolithiasis and prostate or bladder carcinoma.

**Holter Monitoring**

All patients were monitored for 24 hours with portable OXFORD MEDILOG 1 tape recorders. All tapes were analyzed semiautomatically at the department of cardiology in Rotterdam. All dysrhythmias that were observed in the recordings of both TIA and control patients were printed out on standard ECG paper, and submitted for a blind review to a cardiologist (APJK).

**Classification of Dysrhythmias**

All tape reports were reviewed for dysrhythmias which are definitely related to cerebral embolism, such as atrial fibrillation or atrial flutter. As the sick sinus syndrome is possibly related to embolism, the tapes were also reviewed for this disorder, which was defined according to Abdon et al as the presence of one of the following: (1) combined sinus bradycardia and sinus arrhythmia with a difference in consecutive cycles of 20% or more and ≤ 50 beats per minute (bpm), or (2) regular sinus bradycardia of ≤ 45 bpm when awake, or (3) sinoatrial block, or (4) sinus arrests of ≥ 1.5 seconds, all irrespective of drug effects. A combination of the sick sinus syndrome and supraventricular tachycardias (heart rate ≥ 100 bpm), specified as atrial tachycardia if P' waves were visible, was classified as the bradyarrhythmia-tachyarrhythmia syndrome. Premature atrial complexes, designated as sporadic if occurring < 20/hour and frequent if > 20/hour, were also screened. These complexes are not directly related to embolism, but may be harbingers of atrial fibrillation.

**Results**

The prevalence of all dysrhythmias has been summarized in table 2. Five TIA patients showed atrial fibrillation, but four of these had already shown AF on a standard ECG.

Of all dysrythmias, only the episodic sick sinus syndrome occurred significantly more frequently in the TIA patients than in the control population (p < 0.0025). Sick sinus syndrome was the bradytachyarrhythmia type in 14 TIA patients and in three controls (p < 0.01).

Of the 32 TIA patients with episodic sick sinus syndrome nine used drugs known to provoke sinus bradycardia (digitalis 6, beta-adrenergic blocking drugs 3) against three of the 13 control patients, or a similar proportion (three of all used beta-blockers).

The mean age of patients with the sick sinus syndrome in both the TIA and the control population was 62 ± 8.8 years against 60 ± 11.1 of the other patients (0.05 < p < 0.10).

In all patients with multiple ischemic attacks, only one vascular territory was involved. The mean number of attacks in patients with sick sinus syndrome was five, against two in the others (0.05 < p < 0.10).

The presence of clinical evidence of cardiovascular disease among TIA patients with and without the sick sinus syndrome is presented in table 3. None of the...
individual factors indicating cardiovascular disease were significantly more common among patients with sinus node dysfunction. Cardiovascular disease of any kind was more common among patients with sick sinus syndrome (50% against 36.8%) but the difference did not reach statistical significance ($X^2 = 1.57; p > 0.10$).

Because heart disease was relatively rare in the control group (table 1), we investigated whether this might still explain the excess of sick sinus syndrome in TIA patients. Table 4 shows that the difference in sinus node disease is significant only in the patients without obvious heart disease.

Carotid angiography was performed in 35 patients with TIA. An atheromatous lesion corresponding to the neurological symptoms was found in seven of the twelve patients with sick sinus syndrome and 14 of the 23 without it. A normal angiogram was found in three and six patients, respectively (differences not significant).

### Discussion

In this study of 100 patients with transient focal ischemic attacks Holter monitoring showed atrial fibrillation in five patients, against two from a group of 100 age and sex-matched control patients. In four of the five TIA patients AF was previously known from the history or standard ECG. In this respect the diagnostic gain is small, in accordance with the findings of Come et al.9

However, mild and episodic forms of sick sinus syndrome, which might also be related to cerebral embolization,9 were found in 32 of the TIA patients against 13 in the control group ($p < 0.0025$). The bradyarrhythmia-tachyarrhythmia syndrome was definitely related to embolism,9 were found in 32 of the TIA patients against 13 in the control group ($p < 0.0025$).
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portion of sick sinus syndrome in the TIA patients
(32%) is similar to the findings of Abdon et al. It is not
clear whether the relationship is causal or indirect. A
common factor such as atherosclerosis might induce
both TIAs and sinus node dysfunction, although the
relationship was not found in patients with ischemic
heart disease. Unlike Abdon et al. we could not find
other indices of a cardiac source of emboli in patients
with sinoatrial disease, such as an excess of normal
carotid angiograms or multiple foci of the TIAs. On
the other hand, preliminary data indicate that these
transient dysrhythmias predispose to cerebral emboli-
zation.9 Prospective studies are necessary to unravel
the association between sinus node disease and TIAs.
If a causal relationship is confirmed, then clinical trials
of therapeutic measures such as pacemaker implant-
tation, withdrawal of responsive drugs and/or antiarrhythmic drug treatment in the prevention of stroke in
TIA patients with sinus node disease are justified.

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One might argue that the preponderance of sinus
node dysfunction in the TIA patients merely reflects
the lower prevalence of cardiovascular disease in the
control group. However, we found that the difference
in sick sinus syndrome between the two groups was
significant only in patients without overt heart disease.
Although it is impossible to exclude a similar relation-
ship with heart disease, because of the small number of
such patients in the control group, this finding makes it
unlikely that the different prevalence of heart disease
among TIA and control patients accounts for the ob-
served difference in sinus node dysfunction. Another
possible objection might be that the control patients
were investigated a few years later than the TIA pa-
ients. Drug use, however, was not responsible. Fur-
thermore, all tapes were analyzed by the same person
and all recordings were blindly reviewed by one cardiologist.

In conclusion, we found an association between
transient sinus node dysfunction and TIAs.
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