

ABSENCE EPILEPSY IN MALTA

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Introduction

Absence epilepsy (AE), more commonly known as petit mal, is characterised by absences with bilaterally symmetrical and synchronous 2-4Hz spike-and-slow waves on the EEG. It is a relatively uncommon type of epilepsy, occurring most often in children, and accounting for 5% - 10% of all childhood seizures.

The typical absence consists of a momentary disturbance of consciousness during which the patient stares blankly for a few seconds. Other symptoms, namely mild clonic components, atonic and tonic components, autonomic phenomena, may also be associated with absences.

Absence epilepsy is often described as benign and rarely continues into adult life. However a high incidence of generalised tonic clonic seizures (GTCS) has been reported in absence patients, leading to persistence of seizures after adolescence. Modern treatment of AE includes ethosuximide and the more recent drug, sodium valproate.

Methodology

Study I

The incidence of Absence Epilepsy in Malta

Records of the EEGs performed at the Neurophysiology Department at St. Luke's Hospital in the years 1985 - 1991 were reviewed, and patients who had recordings of bilaterally symmetrical and synchronous 2-4Hz spike and discharges (2Hz SP-W), were included in the study.

Only records of the request forms of EEGs performed in 1990 and 1991 were kept at the Neurophysiology Department. These were reviewed for cases where the presenting complaints were absences, and where the EEG failed to show any changes. The medical histories of these patients were checked for AE.

The Schedule V forms of patients with chronic illnesses applying for the supply of free drugs in 1991, kept at the Almoner's Section at St. Luke's Hospital, were reviewed for patients on treatment with ethosuximide or sodium valproate. The medical histories of these patients were sent for and checked for absence epilepsy.

Study II

Clinical aspects of Absence Epilepsy in Malta

The medical histories of the patients found in Study I, were reviewed. Data on age, age at onset of AE, family history, seizure control and treatment was collected.

Study III

Patient Interviews

The main aims of the interviews with patients with absence epilepsy were:

- a) to assess patient compliance
- b) to identify the side-effects experienced by the patients
- c) to assess the patient-pharmacist relationship

An appointment for an interview at the Neurology Out Patient's Clinic at St. Luke's Hospital was sent by post to all mentally normal absence patients; these were mostly adults who regularly attend this clinic.

Children with AE were simply interviewed when they attended for a regular appointment at the Children's Out Patient Clinic.

Study IV

Urinalysis of samples from Patients taking ethosuximide

A urine sample was collected from each of the six patients interviewed in Study III who were on treatment with ethosuximide.

The metabolites and unchanged drug were extracted from the urine with chloroform and four different fractions were separated using thin layer chromatography. The four different bands were given a number from I to IV, I being given to the most polar fraction remaining closest to the original point of application of the sample, and IV being the fraction which migrated furthest from the origin. The R_f values of the four different fractions were calculated (Table 1).

The four different bands on the chromatogram were scraped off separately so as to isolate the four extracted fractions.

The different fractions were extracted from the silica into the chloroform, and an IR spectrum was obtained for each fraction.

The IR spectra showed the presence of the succinimide ring characteristic of ethosuximide and its metabolites in these four fractions, and also in the polar residue left at the original point of application of the sample.

Table 1: Rf values of urine extracts

| Extracts | Rf values obtained from TLC of the different sample extracts | |
|----------|--|---------|
| | Range | Average |
| I | 0.035 - 0.063 | 0.046 |
| II | 0.082 - 0.142 | 0.113 |
| III | 0.481 - 0.590 | 0.541 |
| IV | 0.887 - 0.944 | 0.920 |

Results:

Study 1: Incidence of Absence Epilepsy in Malta

In the period 1985 - 1991, 34 patients were diagnosed to have EEG recordings of 3Hz SP-W discharges for the first time. 7 of these patients had seizures other than absences. Therefore, in the seven year period, 27 patients were diagnosed to have AE, giving an average of 39 new cases of AE annually .

There was a mean annual incidence of 1.1 cases per 100,000 people. Since 26 out of 27 patients were children under 16 years of age, there was a mean annual incidence of 4.2 cases per 100,000 children aged 0 - 15 years of age (Table 2).

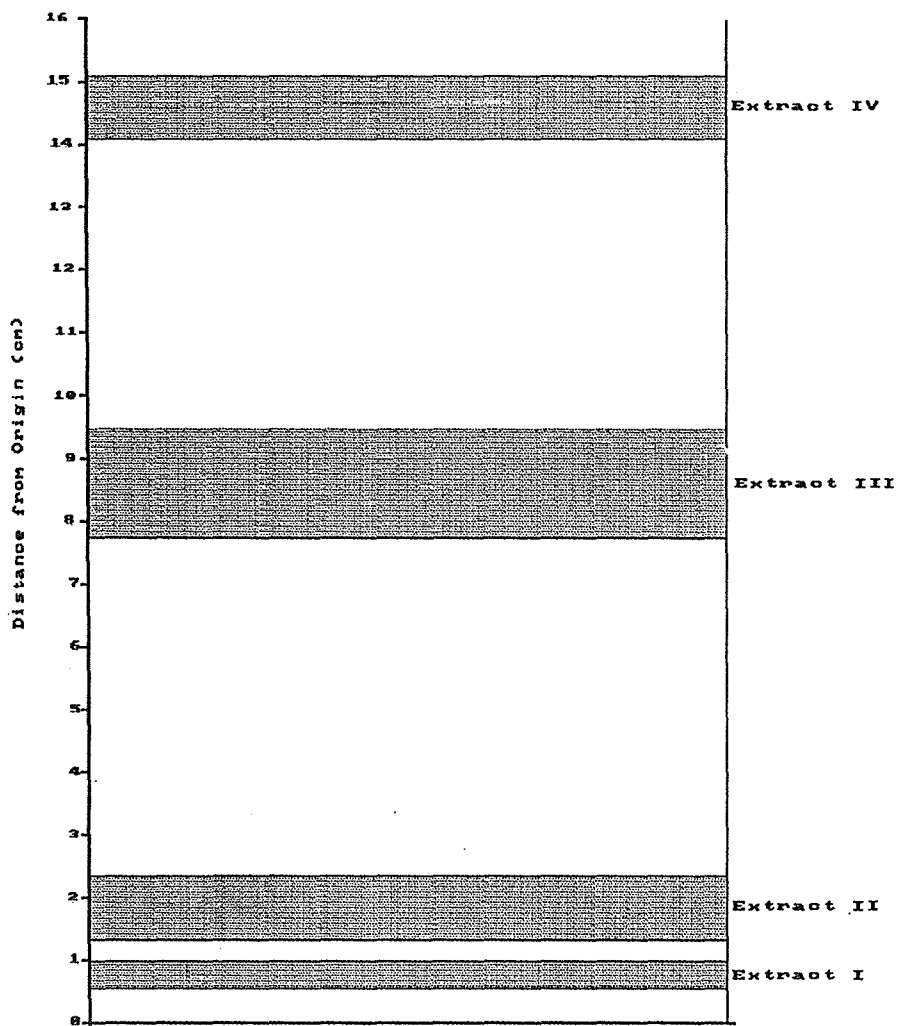


Fig 1
TLC Chromatogram of Urine extracts

Table 2: Comparison of Incidence of AE in Malta with that in other countries

| Age group | Incidence of AE/100,000 population | |
|--------------|------------------------------------|---------|
| | Malta | Sweden |
| children | | |
| 0 - 15 years | 4.2 | 7.0 |
| | | Denmark |
| all ages | 1.1 | 0.8 |

Study II

66.7% (n=18) of the patients with AE were found to suffer only from absences, 22.2% (n=6) have GTCS in addition to absences and 11.1% (n=3) were patients with diffuse brain damage some of which have other seizure types in addition to absences.

A history of seizures among close relatives (parents, siblings, grandparents and parents' siblings) was found in 39.1% of the patients and slightly more frequent in children with initial absences followed by GTCS. This is high compared to the family history of seizures found in children with AE in Sweden (Table 3). Febrile convulsions had preceeded in children with initial GTCS.

In 24 patients found to suffer from absences only valproate was used as the drug of first choice in 83.3% (n=20). It was efficient in 80% of these cases (n=16). However, 10% (n=2) of the patients became seizure-free with ethosuximide monotherapy, 5% (n=1) required a combination of both drugs for control and the remaining case (5% preferred single absences to anti-epileptic drug therapy. Ethosuximide as the initial therapy for AE was used in 16.7% of the cases (n=4). It was efficient in 50% of the patients (n=2), with the other patients (n=2) requiring polytherapy for seizure control (Table 4).

Table 3: Family history and history of febrile seizures in AE patients in Malta and Sweden

| Family History | Clinical Subgroups | | | Total % (n) |
|-------------------------------|----------------------------|------------------------|--------------------|-------------|
| | Absences only + GTCS % (n) | Initial absences % (n) | Initial GTCS % (n) | |
| Maltese Study (1992) | 35.3(6) | 66.7 (2) | 33.3 (1) | 39.1 (9) |
| Swedish Study (1988) | 14 | 29 | 10 | 19 |
| Febrile Seizures % (n) | | | | |
| Maltese Study (1992) | 11.8 (2) | 33.3 (1) | 33.3 (1) | 17.4 (4) |
| Swedish Study (1988) | 11 | 13 | 50 | 15 |

Table 4: Treatment and response in 24 patients suffering from absences +/- GTCS

| Drug(s) | No. of patients on initial therapy | | Response to initial therapy | | Final Nil | Final treatment and response | |
|-----------------|------------------------------------|------|-----------------------------|----------------|----------------|------------------------------|------|
| | n | % | Good | Poor | | Good | Poor |
| VPA | 20 | 83.3 | 16 | - | 4 ^a | 16 | - |
| ESM | 4 | 16.7 | 2 | 1 ^b | 1 ^c | 4 | - |
| VPA + ESM | - | - | - | - | - | 2 | - |
| VPA + ESM + CZP | - | - | - | - | - | - | 1 |

a: 2 patients controlled with ESM
1 controlled with VPA + ESM combination

- 1 preferred absences to drug therapy
b: controlled on ESM + VPA combination
c: controlled on ESM + VPA + CZP combination

Table 5: Seizure control in patients suffering from absences only and those with GTCS in addition to absences

| Seizure type | No. of patients controlled with Treatment | | | |
|------------------------|---|------|---------------------|------|
| | 1 year after start | | 2 years after start | |
| | n | % | n | % |
| absences only n=18 | 15 | 83.3 | 17 | 94.4 |
| absences + GTCS n=6 | 1 | 16,6 | 3 | 50.0 |

Study III: (i) Patient Compliance

(The interview was carried out with 72% (n=18) of the 25 patients who qualified for the interview).

Only 16.7% (n=3) of the patients interviewed were found to be non compliant. The frequency of missed doses tended to be higher in adult patients, in those who have been epileptic for 10 years or longer, in patients on polytherapy and in those taking frequent daily doses.

(ii) Side Effects in Absence Patients

66.7% (n=12) of the patients interviewed experienced some kind of adverse effect due to their medication. 77.8% (n=7) of the patients on polytherapy as compared to 55% (n=5) of those on monotherapy, have suffered from side effects.

Only 11.1% of the patients interviewed (n=2) had been informed of the side-effects of their medication by the pharmacist, whereas 46.2% of the patients (n=9) became aware of these side-effects through reading product literature.

(iii) The Patient-Pharmacist relationship

Only 27.8% (n=5) of the patients interviewed had informed the community pharmacist in their home town or village, about their condition, and only 16.7% (n=3) asked the dispensary pharmacist advise about their medication. Older patients, patients who have been epileptics for 10 years and longer and patients who had GTCS in addition to absences were less likely to consult the pharmacist for advice or information.

Discussion

Although absence epilepsy is often described in textbooks as benign and seldom continues beyond adult life, this is a rather optimistic outlook regarding the prognoses of AE.

An unfavourable outcome of AE is associated with the appearance of GTCS. In this study 6 patients were found to have been suffering from AE for 20 - 40 years (median 33 years). These patients have GTCS in addition to absences, and the onset of GTCS was in the range between 5 - 21 years (median 16 years) after onset of absences.

Recurrences of seizures usually occur within the first 2 years of treatment, but recurrences of up to 20 years after termination of treatment have been reported.

Therefore, good social adaption is important in the epileptic. This is effected by the patient's own attitude to epilepsy, its severity and its impact on their lives. Most absence epilepsy patients wanted to know more about their condition, and its treatment, mostly through leaflets but even through attending special lectures, and watching special TV programs or videos. 22.2% (n=4) of the patients interviewed, spontaneously suggested that a Maltese Epilepsy Society should be set up.

Yet, only 27.7% (n=5) have informed their community pharmacist about their condition and asked him for advice and information. The pharmacist in the community, however is in an ideal position to help these epileptics with more information about epilepsy and their medication, so as to manage better their condition.

References

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