Original article

Treatment of Epilepsy in Rural Ethiopia: 2 Year Follow-up

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Abstract

Background: Epilepsy is the commonest cause of neurological disability in rural Ethiopia. Untreated epileptic seizures read to physical injury and psychosocial morbidity. Frequent seizures have a determining effect on education, employment and marital life.

Objective: To review outcomes of a two years follow-up study.

Methods: The study was conducted in December 2001 at the epilepsy clinics at five health centers in the region around Gondar in northern Ethiopia. The case records of patients who had been followed up for two or more years were reviewed. Patients who missed 3 or more consecutive clinic visits were not included and were classified as defaulters.

Result: Forty nine percent of patients were still under follow-up after 1 year and this fell to 38% at 2 years. There was marked variation between HCs with 73% still under follow-up at 2 years at two HCs. Of those still under follow-up at 2 years 48% had been seizure free for 1 year or more and another 34% experienced a >90% reduction in seizure frequency. 87% were treated with phenobarbitone monotherapy (median dose: 150mg/day). Age of onset of epilepsy before age 15 years and seizure frequency of one or more seizures per week prior to treatment were associated with failure to achieve one year remission. Duration of epilepsy and seizure type did not affect seizure control. Review of the records of 318 patients who had defaulted from follow-up at one HC showed that seizure control at the time of default was similar to that achieved by the patients still attending with only 5% poorly controlled compared with 3.9%. The mean travelling time to the HC was 4.1hrs for the defaulters and 5.4hrs for those still attending.

Conclusion: Good follow-up rates can be achieved even after two years and that response to treatment in those who remain under follow-up is very good falling little short of what is seen in more developed countries. [*Ethiop.J.Health Dev.* 2004;18(1):31-34]

Introduction

Epilepsy is the commonest cause of neurological disability in rural Ethiopia (1). In under-developed communities people with epilepsy are stigmatised due to ignorance and superstition (2). Untreated epileptic seizures lead to physical injury and psychosocial morbidity (3,4). Where open fires are used for cooking, epilepsy is classically associated with burns. Frequent seizures have a detrimental effect on education, employment and marital life. Epilepsy is also associated with increased mortality (5).

Despite the availability of phenobarbitone an inexpensive and effective treatment, 87-98% of people with epilepsy living in rural areas of Ethiopia are untreated (4,6). Ninety percent of those not receiving treatment seem to be unaware that medical treatment exists (4). A study performed in Kenya showed that patients with a history of an untreated seizure were just as likely to respond to treatment as those with recent onset seizures; 53% of patients became seizure free and another 26% experienced a worthwhile reduction in seizure frequency (7).

In April 1998, we set up nurse-led epilepsy clinics in five rural health centres in the region around Gondar in northern Ethiopia. Existing healthcare infrastructure was used and the clinics were integrated with the routine services of the health centres with few additional resources.

Phenobarbitone is the only antiepileptic drug reliably available in rural areas and was the mainstay of treatment. In the first 18 months of the programme, a total of 813 patients were registered and started on treatment. The clinical characteristics of the patients have been reported previously (4). Here we report on a two years follow-up.

Methods

This study was performed in December 2001 at the epilepsy clinics at the five health centres (Aykel, Dabat, Debark, Koladuba and Tseda), which form part of the Gondar non-communicable disease project. The case records of patients who had been followed-up for two or more years were reviewed. Patients who missed 3 or more consecutive clinic visits (or who had not attended for more than 6 months) were not included and were classified as defaulters.

At the time of initial registration basic demographic details, seizure history, risk factors, treatment history and

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examination findings were recorded. Seizure classification was on clinical grounds according to the International League Against Epilepsy Guidelines for epidemiological studies on epilepsy (8). All patients with active epilepsy were started on phenobarbitone. In adults the starting dose was 50-60mg and in children 1-2mg/kg. The patients were asked to attend every two months. Unless non-compliance

was suspected, the dose was gradually increased according to response up to a maximum of 240mg per day, if tolerated.

If phenobarbitone was ineffective or not tolerated, limited supplies of phenytoin were available. At each visit, after registration, seizure frequency, drug treatment, drug dosage, adverse effects and any complications (e.g. injuries and episodes of status) were recorded on a structured follow-up chart. The level of seizure control was graded: seizure free for 1year or more, >90% reduction in seizure frequency, >50% reduction in seizure frequency and <50% reduction in seizure frequency.

Patients who were seizure free were compared to those who had not achieved a remission of one year with respect to age of onset, duration of epilepsy, seizure type and seizure frequency prior to treatment. Chi square test for proportions was used to compare the various patient groups and odds ratios with 95% confidence intervals were calculated.

The records of the patients who had defaulted from followup at the health centre at Aykel were examined to determine the level of seizure control at the time of default and to establish the journey time to the health centre.

Results

Of the 813 patients with active epilepsy registered before December 1999, 49% were still under regular follow-up 1 year after registration and this fell to 38% at two years. There was, however, marked variation between health centres with, 73% still under follow-up at 2 years at two of the health centres (Table 1).

Table 1: **Number of patients at each health centre still under follow-up after 2 years**

Health Centre	No. of patients Registered	No. of patients under Follow-up at 2yrs (%)
Tseda	30	22 (73)
Koladuba	80	58 (73)
Dabat	171	74 (43)
Debark	85	29 (34)
Aykel	447	129 (29)
Total	813	312 (38)

Table 2: **Clinical characteristics of patients still under follow-up after 2 years and all patients registered ≥2 years ago**

	Patients under follow-up 2 years. n=312	**All patients registered ≥2 years ago. n=813**
Sex (M:F)	1.5:1	1.5:1
Median age at onset (range)	14 yrs (2months-73 yrs)	14yrs(at birth to 75yrs)
Median duration of epilepsy (range)	5 yrs (1 month-47 yrs)	4 yrs (1 month-50 yrs)
Seizure type	80% generalised 20% partial	81% generalised 19% partial
Seizure frequency before treatment	37% ≥1/week 56% 1-3/month	33% ≥1/week 54% 1-3/month

Of those still under follow-up after 2 years, 60% were male. The median age at onset of seizures was 14 years (range 2 months to 73 years). The duration of epilepsy ranged from 1 month to 47 years (median 5 years). 80% were classified as having generalised seizures and 20% partial seizures. Before treatment 56% were experiencing between one and three seizures per month and 37% were having one or more seizures per week. This profile is very similar to that of the whole group of 813 registered patients (Table 2).

Eighty seven percent of patients were treated with phenobarbitone monotherapy at a median dose of 150mg daily and only 6% were on doses in excess of 200mg daily. The majority of the remainder were on a combination of phenobarbitone and phenytoin, with less than 1% on phenytoin monotherapy. Adverse effects were rarely reported.

Forty eight percent had been seizure free for one year or more and altogether, 82% had experienced a >90% reduction in seizure frequency (Table 3). Age of onset of epilepsy before age 15 and seizure frequency of one or more seizures per week prior to treatment were associated with failure to achieve one year remission. Duration of epilepsy and seizure type did not affect seizure control (Table 4). Two percent reported an episode of status epilepticus during the course of follow-up.

Table 3: **Degree of seizure control 2 years after starting treatment**

Seizure Control	Number of patients	% of patients
Seizure free for ≥ 1 year	150	48
>90% seizure reduction	106	34
50-90% seizure reduction	41	13
<50% seizure reduction	15	5
Total	312	100

The defaulters from the clinic at the health centre at Aykel accounted for 63% of the patients lost to follow-up. The follow-up charts revealed that 68% had been seizure free on one or more consecutive clinic visits before they defaulted and only 5% had experienced a <50% reduction in seizures. Their mean journey time (hours walk) to the health centre was 4.1 hours compared with 5.4 hours for those still under follow-up after 2 years.

Discussion

The epidemiology and clinical characteristics of epilepsy in rural Ethiopia have been described previously (1,3,4,6), however, there have been no studies looking at treatment outcome. We have shown that it is possible to achieve good seizure control in nurse-led epilepsy clinics in rural health centres with phenobarbitone as the mainstay of treatment. Adherence to follow-up after two years was as high as 73% at some health centres, but at others default from follow-up was a significant problem.

Overall, the patients still under follow-up after two years accounted for only 38% of the patients originally registered, but they were very similar to the group as a whole in terms of age of seizure onset, duration of epilepsy, seizure type and seizure frequency before treatment. Although seizure control might have been expected to be worse amongst patients who had defaulted, we found that seizure control was good with 68% seizure free at one or more consecutive visits before default. Nevertheless, conclusions relating to the patients remaining under followup after two years can only be generalised with caution.

Table 4: **Factors associated with failure to achieve a 1 year remission**

	Seizure free for ≥1 year	Not seizure free	Odds ratio (CI)
Age of onset (<15 years)	67	95	1.76 (1.09-2.82)*
Duration of epilepsy (>5 years)	59	79	1.47 (0.91-2.36)
Seizure type (partial seizures)	27	36	1.30 (0.88-1.45)
Seizure frequency before treatment (≥1/week)	41	75	2.29 (1.39-3.79)**

* p<0.05
** p<0.01

The proportion of patients still under follow-up after 2 years who were seizure free (48%) is similar to that observed in studies performed in Kenya, Tanzania and Malawi (52-56%) (5,7,9). In a study from Nigeria, only 30% were seizure free, but the patients were attending a university college hospital and it is possible that the patients had more severe epilepsy that had not responded to treatment in the community (10). Default rates in these studies were 18-42% and follow-up was often for less than 2 years. Overall, 92% of our patients achieved a >50% reduction in seizures compared with 79-88% in the studies from Kenya, Tanzania and Malawi (5,7,9).

In keeping with other studies, duration of epilepsy did not influence seizure control (7), indicating that even those with a long history of untreated seizures living in rural

communities may gain significant benefits from treatment. We also found that seizure type did not affect response to treatment. Seizures were classified on clinical grounds only and reliable descriptions of seizures were often difficult to obtain. Twenty percent had seizures with clinical evidence of partial onset, but this is likely to be an underestimate and misclassification of seizures, which could have influenced this result. A prospective population based study performed in the UK, however, also showed that seizure type had no significant effect on the chances of achieving remission (11).

Age of onset before 15 years and frequent seizures prior to treatment were both associated with failure to become seizure free. These findings are best explained on the basis that severe epilepsy, which is refractory to drug treatment, presents earlier and with more frequent seizures, rather than supporting the notion that "seizures beget seizures"(12). This explanation would be consistent with the observation that duration of epilepsy did not affect seizure outcome.

In rural areas of Ethiopia and many other developing countries phenobarbitone is still the only affordable and reliably available antiepileptic drug, and the majority of our patients were managed with phenobarbitone monotherapy. There is no evidence that other antiepileptic drugs including the newer drugs are any more effective than phenobarbitone and a study performed in Kenya showed that both efficacy and tolerability of phenobarbitone were similar to carbamazepine (7).

When a patient proves resistant to drug treatment, there is a temptation to continue increasing the dose regardless of adverse effects particularly when other treatment options are limited. Simple treatment guidelines given to the health centre nurses were effective and doses of phenobarbitone rarely exceeded 200mg per day.

In patients treated with phenobarbitone, withdrawal seizures and risk of status epilepticus are of concern

particularly if there is poor compliance or supplies are unreliable (13). Since we established the clinics in 1998 drug supplies have been maintained without interruption and status was reported in only 2% during the period of follow-up.

Although follow-up rates after two years were high at some health centres, overall default was a major problem. The reason for the high default rate is unclear. Treatment failure and adverse effects of treatment may have caused some patients to revert to traditional remedies, but these factors are likely to be common to all patients and are unlikely to account for the marked variation between health centres. This is supported by the finding that the majority (68%) of the patients who defaulted from the health centre at Aykel were seizure free at the point of default. The possibility that the clinics were inaccessible for some patients was also considered, but at Aykel, which had the highest default rate, the journey time was similar for patients who had defaulted and for those who remained under follow-up. Factors other than simply distance may, however, determine whether patients can get to the clinics. Many patients, particularly those still experiencing seizures, cannot travel unaccompanied and unless family or friends can be released from domestic or farming duties, they are unable to attend. We often observed relatives collecting drugs on behalf of patients to avoid the cost of transport for two people. We have also seen representatives from villages far from the health centre collecting drugs for several patients to minimise the numbers having to travel and to reduce costs.

Unavailability and cost of treatment have been suggested as potential reasons for default (10,14), but we cannot attribute default to this because there was no interruption to the supply of phenobarbitone to the health centres and in line with health centre policy patients unable to afford treatment were given treatment without charge. Migration is considered unlikely to be a reason for default in this region. Other potential causes yet to be examined include differences in education and support provided at different health centres, death either epilepsy related or from other causes and the less likely possibility of spontaneous remission. Locating defaulters in remote rural areas in order to establish causes of default is, however, a challenging problem.

Further work is required to establish the most important determinants of default, but we have shown that good follow-up rates can be achieved even after two years and that response to treatment in those who remain under follow-up is very good falling little short of what is seen in more developed countries. Furthermore, these results have been obtained using existing healthcare infrastructure with few additional resources.

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