Treatment with phenobarbital and monitoring of epileptic patients in rural Mali

K. Nimaga,[1] D. Desplats,[2] O. Doumbo,[3] & G. Farnarier[4]

Objective To assess the efficacy of phenobarbital treatment for epileptic patients in rural Mali.
Methods Epileptic patients were treated at home with phenobarbital at daily dosages ranging from 50 mg for children to 200 mg for adults and their condition was monitored. Advice was given to patients, their families, and the village authorities in order to achieve compliance. An uninterrupted supply of generic phenobarbital was provided and a rural physician made two follow-up visits to each village to ensure that the drug was taken in the correct doses. The physician gave information to the population, distributed the phenobarbital in sufficient quantities to cover the periods between visits, and monitored the patients' responses to treatment. During the first year the physician visited the patients every two months. The frequency of visits was subsequently reduced to once every four months.
Findings In the six months preceding treatment the average rate of seizures among patients exceeded four per month. After a year of treatment, 80.2% of the patients experienced no seizures for at least five months. A total of 15.7% of patients experienced a reduction in seizures. In many cases no further seizures occurred and there were improvements in physical health, mental health and social status. There were very few side-effects and no cases of poisoning were reported. The cost of treatment per patient per year was US$ 7 for generic phenobarbital and US$ 8.4 for logistics.
Conclusion Low doses of phenobarbital were very effective against epilepsy. However, there is an urgent need for programmes involving increased numbers of physicians in rural areas and, at the national level, for the inclusion of epilepsy treatment in the activities of health care facilities. Internationally, an epilepsy control programme providing free treatment should be developed.

Keywords Phenobarbital/therapeutic use/administration and dosage; Epilepsy/drug therapy/epidemiology; Patient compliance; Treatment outcome; Case management; Rural population; Mali (*source: MeSH, NLM*).

Mots clés Phénobarbital/usage thérapeutique/administration et posologie; Epilepsie/chimiothérapie/épidémiologie; Observance prescription; Evaluation résultats traitement; Gestion cas; population rurale; Mali (*source: MeSH, INSERM*).

Palabras clave Fenobarbital/uso terapéutico/administración y dosificación; Epilepsia/quimioterapia/epidemiología; Cooperación del paciente; Resultado del tratamiento; Manejo de caso; Población rural; Malí (*fuente: DeCS, BIREME*).

Bulletin of the World Health Organization 2002;80:532-537.

Voir page 536 le résumé en français. En la página 537 figura un resumen en español.

Introduction

In 1996 a campaign was launched by WHO, the International League against Epilepsy and the International Bureau for Epilepsy to "bring epilepsy out of the shadows" (*1–4*). For biogeographical, cultural and, above all, economic reasons, epilepsy is more prevalent in developing countries than in industrialized ones (*5–7*). Its prevalence varies widely from place to place; for example, in a rural area close to Bamako, Mali, the overall prevalence was 13.35 per 1000 but there were large differences between villages (*8*).

Managing epilepsy in rural Africa is particularly difficult. Diagnosis may be impossible because of a shortage of expertise and the absence of the most basic diagnostic equipment. Also, case management may be hampered by the unavailability of antiepileptic drugs, the inaccessibility of locations, financial constraints, inappropriate prescriptions and poor compliance.

Nevertheless, effective care is possible. At the risk of missing some cases, diagnosis often depends on the use of clinical data and the least expensive drugs, particularly phenobarbital or phenytoin. Monitoring of patients is the cornerstone of any successful treatment. It should ensure adequate drug supplies, proper compliance, i.e. uninterrupted and correct doses, a positive effect, and the avoidance of changes in prescription because of undesirable side-effects. However, such follow-up is often impossible because the vast majority of people in rural Africa cannot afford to visit a doctor frequently nor even to attend the most rudimentary health care facilities.

In this paper we describe a programme of case management and monitoring of epileptic patients in rural Mali.

Methods

An anthropological survey on epilepsy was conducted in a hospital and an urban area of Mali from May to December 1996 (*9*) and another began in the countryside in November 1997 in the areas where the subsequent phases of the study were implemented (*10*, *11*).

[1] Rural Physician, Santé Sud, Bamako, Mali.
[2] Programme Director, Santé Sud, Marseilles, France.
[3] Head, Department of Epidemiology of Parasitic Diseases, Faculty of Medicine; and Head, Santé Sud, Bamako, Mali.
[4] Head, Service de Neurophysiologie Clinique, CHRU Hôpital Nord, 13915 Marseilles Cedex 20, France (email: gfarnarier@mail.ap-hm.fr). Correspondence should be addressed to this author.
Ref. No. **00-0781**

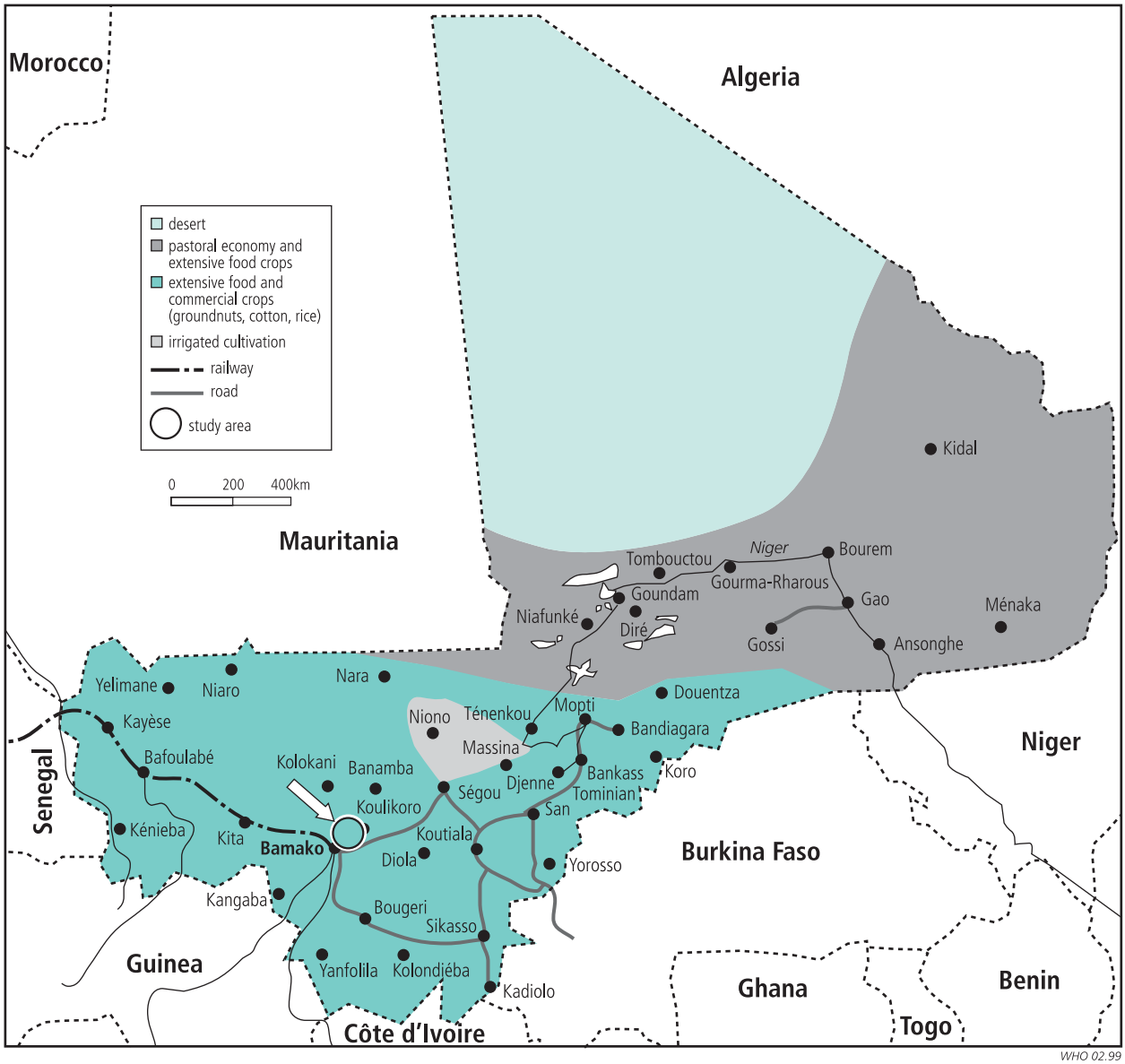
In May 1998 a door-to-door epidemiological survey of 5243 individuals aged ⩾7 years was conducted in 18 villages around Tyenfala, in Koulikoro district, and Baguineda, in Kati district, ca 40–100 km to the east of the capital, Bamako (Fig. 1). This phase included a demographic study, the screening of epileptic patients, a survey of the prevalence of epilepsy, research on risk factors, and clinical and biological investigations (*6*, *12*, *13*). Epilepsy was diagnosed in 70 persons.

New cases were reported spontaneously in neighbouring villages, and consequently 136 patients, including children under 7 years of age, are now being treated. The 34 villages currently being covered are scattered along the River Niger in areas between the towns of Bamako and Koulikoro. Access to these areas can be problematic, especially during the rainy season: Baguineda is an agricultural area subject to heavy flooding, while Tyenfala comprises hillside villages accessible only with difficulty.

The target group under study after a year of treatment included 42 men and 54 women of mean age 27.1 years ± 13.8 (range, 5–71 years; median, 28.5 years). The patients were monitored by a rural physician who visited their homes. Monitoring relied on regular visits by the physician. The physician or an aide informed the population of each forthcoming visit. A few days later the physician arrived by car or motorcycle, depending on the season, in order to bring supplies, conduct monitoring, and provide treatment. Each trip required the physician to travel about 1300 km.

The average duration of phenobarbital treatment was 11.5 ± 2.6 months (range: 5–13 months). The daily dose ranged from 50 mg for children to 200 mg for adults. The adult dose was increased or decreased by amounts of 50 mg. The average daily dose was 110 ± 30 mg. The protocol was established on the following basis: the patients and their families were properly counselled via the village authorities in order to ensure correct compliance with treatment; the antiepileptic drug was provided regularly and in sufficient quantities to meet the requirements of each patient between visits; proper administration of the drug was ensured; and data

Fig. 1. **Map showing study area in Mali**



were collected on seizures, general status, and side-effects. The antiepileptic drug, generic phenobarbital, supplied in boxes of 1000 tablets (100 mg per tablet), was chosen because of its low cost and effectiveness in controlling seizures. The doses needed for the period between visits were packaged in waterproof plastic sachets and left in the care of each patient.

During the first year of treatment, from January 1999 to January 2000, a physician visited each patient every two months. This was subsequently reduced to one visit every four months in the light of the satisfactory results obtained. In order to simplify the work of the physician and ensure optimal data collection, a monitoring chart was completed during each visit.

Results

Clinical data (see Table 1)

During the six months preceding phenobarbital treatment, the average number of seizures per patient per month was 4.2 ± 8.3 (range: 0–30). Some patients had several seizures per day. Signs of general seizures were shown by 70% of patients and partial seizures by 22%; there was secondary generalization in over three-quarters of the latter cases. The type of seizure was indeterminate in the remaining cases. Fewer than 20% of epilepsy cases were regarded as symptomatic, i.e. the result of an illness, or affecting patients with signs of disorders of the central nervous system. The other cases were considered to be cryptogenic or idiopathic. The lack of diagnostic resources explained why generalized seizures far outnumbered partial seizures and why cases of the cryptogenic type of epilepsy significantly outnumbered those of symptomatic epilepsy.

In most cases, the patients' medical histories included infectious illnesses. To a lesser extent perinatal illnesses were represented and, even more rarely, trauma-related disorders. Neurological signs were observed in some patients. Although these case histories were not necessarily linked to the occurrence of epilepsy, the condition appeared in seven patients following a disease episode which, in most cases, was infectious.

For over half the patients there was a family history of epilepsy and for a quarter of them there was evidence of consanguinity among their parents. It should be noted that the rate of consanguinity was probably greatly underestimated.

Table 1. **Clinical data**

	No. cases[a]	No. patients[b]
Types of seizures		
Generalized seizures	67	96 (69.8)[c]
Partial seizures without secondary generalization	5	96 (5.2)
Partial seizures with secondary generalization	16	96 (16.7)
Undetermined seizures	8	96 (8.3)
Etiology		
Cryptogenic (or idiopathic) epilepsy	80	96 (83.3)
Symptomatic epilepsy	16	96 (16.7)
Medical history		
Infectious	28	92 (30.4)
Perinatal	13	92 (14.1)
Trauma-related	2	92 (2.2)
Neurological signs	12	94 (13)
Secondary epilepsy[d]	7	96 (7.3)
Family history of epilepsy	50	96 (52.1)
Consanguinity among parents	19	76 (25)

[a] No. of epileptic patients who met established criteria.
[b] No. of epileptic patients from whom information on criteria was obtained (of a target group of 96).
[c] Figures in parentheses are the percentage of epileptic patients who met established criteria.
[d] Type of epilepsy arising because of a clearly identified disease episode.

Treatment data (see Table 2)

Almost 60% of the patients had never taken an antiepileptic drug. Furthermore, one-third of those who claimed to have taken such a drug could not give any details, suggesting that in most cases it had not been an antiepileptic. In 86% of cases the drugs had been taken without a medical prescription but had been recommended by relatives or acquaintances. Prescriptions had been made out in one case by a nurse and in four cases by a doctor, followed twice by self-prescription, including self-prescription of another antiepileptic drug.

When the type of antiepileptic drug was specified it was phenytoin in almost 80% of cases, twice combined or alternated with phenobarbital, and once with carbamazepine. In 30% of the cases, phenobarbital was combined or alternated with phenytoin. In one case the drug used was valproic acid and in another it was carbamazepine, also combined or alternated with phenytoin. The drugs were taken without any indication of dosage and without medical supervision. In all cases the treatment was frequently discontinued. Patients who obtained unsatisfactory results often decided to stop taking the drugs altogether. Overall, therefore, it can be assumed either that the patients were not treated at all or that they were not treated properly.

It should be noted that all patients had taken traditional treatments prescribed by their families, friends and traditional healers. These treatments included the use of concoctions, incenses, ointments, as well as the wearing of amulets, and were usually plant- or animal-based. However, they did not prove particularly effective for the control of epileptic seizures.

Approximately 80% of the patients took the drug as prescribed. However, ca 20% failed to comply with or unnecessarily discontinued the treatment. Four patients involuntarily discontinued treatment.

Seizures disappeared completely for over 80% of the patients after they had been receiving phenobarbital for at least five months. The seizures were reduced, i.e. they became fewer and/or less severe, for approximately 16% of the patients, while no change was observed for one patient, despite compliance, and for two patients with poor compliance. Excellent results were obtained for at least 19 subjects who no longer experienced seizures and enjoyed improvements in physical health (better general status, sound sleep), mental health (no further depression or neurotic disorder), and social status (formerly excluded subjects resumed work, formerly rejected wives returned to family home, children were sent to school).

Minor side-effects, i.e. dizziness and drowsiness, were frequently observed at the beginning of treatment. However, they did not continue and the few patients who stopped their treatment because of them soon resumed it. After a year of treatment only three patients experienced adverse effects: rheumatism in two and an allergic skin reaction in the third. However, in the absence of any other antiepileptic drug, these patients decided to continue with the phenobarbital treatment

Table 2. **Treatment data**

	No. cases[a]	No. patients[b]
Treatment history		
Never used an antiepileptic drug	49	85 (57.6)[c]
Used an antiepileptic drug	24	85 (28.2)
May have used an antiepileptic drug	12	85 (14.1)
Self-prescribed antiepileptic drug	31	36 (86.1)
Type of antiepileptic drug (where used)		
Phenytoin	19	24 (79.2)
Phenobarbital	7	24 (29.2)
Carbamazepine	1	24 (4.2)
Valproic acid	1	24 (4.4)
Traditional healing	96	96 (100)
Compliance with phenobarbital treatment		
Proper compliance	75	96 (78.1)
Non-compliance	17	96 (17.7)
Involuntary discontinuation of treatment	4	96 (4.2)
Effects of phenobarbital treatment		
No more seizures for at least five months	78	96 (81.3)
Fewer seizures	15	96 (15.7)
Same number of seizures	3	96 (3.1)
Side-effects after one year	3	96 (3.1)

[a] No. of epileptic patients who met established criteria.
[b] No. of epileptic patients from whom information on criteria was obtained (of a target group of 96).
[c] Figures in parentheses are percentage of epileptic patients who met established criteria.

because of the excellent control of their seizures. No deliberate or accidental cases of phenobarbital poisoning were observed.

Discussion

The crude prevalence of epilepsy (13.35 per 1000) indicated by the epidemiological survey in the study area is consistent with the prevalence of 10–20 per 1000 generally observed in developing countries, but is much higher than the prevalences reported from industrialized countries. Even within the geographical area of our study, the distribution of epileptic patients was not uniform, i.e. some villages had significantly more than others. Considerable variations in the prevalence of epilepsy occur between studies and between geographical regions. Such variations can probably be attributed to certain risk factors, particularly infectious or genetic ones, such as a high incidence of epilepsy in families, even though possible risk factors are common to all family members, and a high rate of consanguinity (*8*).

The prevalence of epilepsy in rural areas of Mali is usually underestimated because of diagnostic problems, namely a lack of exploratory equipment and poor knowledge of epilepsy in the medical profession. Genuine cases of epilepsy may not be correctly diagnosed, e.g. childhood epilepsy and non-motor seizures. Other cases may be concealed for cultural reasons. The present study was undoubtedly affected by such biases.

In general, satisfactory treatment outcomes depend on accurate diagnosis, the administration of an antiepileptic drug suited to the particular type of epilepsy, and regular monitoring. In many developing countries, economic and cultural obstacles prevent these things from happening. Diagnosis and treatment are limited by a lack of resources. Compliance with treatment can be hampered by traditional beliefs. Nonetheless, practically all of these problems can be overcome through the use of inexpensive drugs, proper training of doctors in the clinical diagnosis of epilepsy, and education of the population. Case management is vital; it is essentially domiciliary, the visiting physician providing the drug and monitoring compliance with the regimen. In the present study, satisfactory compliance was attributable to the patients' confidence in the physician, the group effect whereby the patient's family, the village authorities and the local health officials each assumed a share of responsibility, and the favourable outcomes of former patients.

During the 1970s, Gastaut and Osuntokun (*14*, *15*) advocated the use in developing countries of antiepileptic drugs such as phenobarbital, phenytoin and carbamazepine, which were considered to be particularly desirable because of their low cost and the quality of the treatment they provided. Similar arguments are still valid today, despite the discovery of new antiepileptics. Some authors have criticized the use of phenobarbital because of the risk of withdrawal seizures, heightened if supplies are interrupted, the risk of drug abuse, interaction with alcohol, the triggering of suicide attempts, and a high level of toxicity. As a result, phenobarbital is no longer used in developed countries and its continued use in developing countries has been described as a form of discrimination (*16*). However, it has been argued that in poor regions, particularly in rural areas, the price to pay for a drug is its side-effects, and that the choice is not between phenobarbital and a new medicament but between phenobarbital and no treatment at all (*17*). In 1998, India considered phenobarbital to be acceptable as a front-line antiepileptic drug for rural children. There is clear evidence favouring the use of phenobarbital over that of phenytoin (*18–20*).

Phenobarbital, taken in low doses, proved very effective in our study. In fact, around 80% of the patients did not experience any seizures for at least five months. These results are undoubtedly explained by the fact that the vast majority of these patients had not received any previous treatment for epilepsy .

The excellent compliance with the drug regimen among the target epileptic population was mainly attributable to the regular domiciliary monitoring of each patient. Other programmes very similar to ours have produced less than satisfactory results, perhaps because this type of monitoring was not used. Much more variable results are usually obtained where a stock of medicine is handed over to a local official for distribution in the community (*21*). The contributions of the patients' families and village authorities should not be underestimated. Their understanding and acceptance of responsibility for treatment was indispensable in ensuring compliance with the drug regimen. The successful outcomes of former patients served to reinforce the monitoring protocol.

The rural populations of Mali are extremely poor and have great difficulty in accessing reasonably satisfactory health care facilities. Even finding the money to purchase medicine for treating chronic illnesses is not easy. According to 1999 statistics, the per capita gross national product (GNP) (purchasing power parity) was only US$ 740 per year (*22*). Furthermore, there were huge disparities, some rural areas being much poorer than the GNP suggests.

Cost of programme

Treatment was free for all patients under our protocol. The cost of the programme consisted of the price of generic phenobarbital, the remuneration of the physician responsible for monitoring and of an assistant, and logistical expenses. There was a need for an average of 1.1 tablets per patient per day, i.e. 401.5 tablets per patient per year. A box of 1000 generic phenobarbital tablets (100 mg each) cost US$ 6.3 (*23*), i.e. US$ 2.5 per patient per year. The cost of personnel and equipment depended on the amount of time involved and the distance travelled. It took roughly eight days to cover over 1000 km, visit all the villages and see about 100 patients and this cost approximately US$ 915 for three rounds a year. Thus the grand total was approximately US$ 920 for the complete case management of the study patients.

For Mali (population, ca 11 million) it seems reasonable to allow for the case management of a minimum of 10 patients per 1000 inhabitants, i.e. a total of 110 000 patients. Should a country decide to provide treatment, the social costs of epilepsy would have to be factored in. There are direct costs for treatment and lost productivity, and indirect costs attributable to premature deaths, illness and so on. Altogether these costs would amount to approximately US$ 6 million for 10 million inhabitants. For this population the cost of case management, based on a minimum-cost protocol such as ours, would be US$ 1 million.

In order to be feasible in the long term, the comprehensive treatment of epileptic patients in rural areas of Mali would require the implementation of a system with appropriate local, national, and international structures. The proposals discussed below are based on a model that can be applied directly to Mali but which could be adapted in general for other countries in West Africa, or indeed for all developing countries.

Local level

There is a shortage of doctors in rural Africa. In Mali, less than one-third of doctors practise in rural areas, although they are inhabited by more than 70% of the population.

Several epidemiological surveys have shown that epilepsy is much more prevalent in rural than urban areas. The vast majority of people living in rural areas do not visit towns to obtain treatment: they may not be able to afford it, the health care facilities may be inaccessible, and cultural factors may come into play. Consequently, it is imperative to increase the number of physicians serving rural areas.

The management of epilepsy cases should be decentralized and medically supervised. Epileptic patients should be monitored by rural physicians who have received basic training in treating epilepsy and are capable of accurate diagnosis, prescribing appropriate treatment, and ensuring systematic and regular follow-up. All these requirements have to be met in order to ensure the compliance of patients and the effectiveness of treatment.

National level

Epilepsy should be considered a priority disease and should be incorporated into the minimum package of services offered by health centres and be placed on an equal footing with major endemic diseases such as leprosy, tuberculosis, onchocerciasis and dracunculiasis, for which national programmes exist in Mali. It should also be covered in information, education and communication sessions.

These activities are funded by either the state or development partners. The political will of donors in respect of epilepsy should be translated into an agreement on the case management of the disease. This agreement could be signed by rural physicians and the state and/or development partners so as to ensure that some form of compensation is awarded annually for each epileptic patient treated and monitored.

International level

A consensus is required on the need to make epilepsy a priority. An epilepsy control programme providing free treatment for patients, similar to the programmes developed by WHO for the eradication of leprosy and onchocerciasis, should be devised. In this way the campaign slogan "bringing epilepsy out of the shadows" could be transformed into reality. ■

Acknowledgements

Case management was made possible by the financial and logistical support of Santé Sud, a nongovernmental organization, and by the monitoring conducted by a rural physician collaborating with this body. Generic phenobarbital was supplied free of charge by the Institut Rhône-Poulenc Rorer.

Conflicts of interest: none declared.

Résumé

Epilepsie : traitement par le phénobarbital et surveillance des patients en milieu rural au Mali

Objectif Evaluer l'efficacité du traitement des épileptiques par le phénobarbital en milieu rural au Mali.

Méthodes On a traité à domicile des épileptiques avec du phénobarbital administré à des posologies quotidiennes allant de 50 mg pour les enfants à 200 mg pour les adultes et on a assuré leur suivi. Des informations ont été fournies aux patients, à leur famille et aux responsables villageois pour une bonne observance du traitement. L'approvisionnement en phénobarbital sous forme générique a été assuré sans interruption et un médecin de campagne a fait deux visites de suivi par village pour vérifier la prise du médicament aux doses correctes. Le médecin a informé la population, distribué le phénobarbital en quantités suffisantes pour couvrir les périodes entre les visites et surveillé les réactions des patients au traitement. Au cours de la première année, le médecin est passé tous les deux mois, puis la fréquence des visites a été réduite à une fois tous les quatre mois.

Résultats Au cours des six mois précédant le traitement, la moyenne mensuelle des crises a été supérieure à quatre. Après un an de traitement, 80,2 % des patients n'avaient pas eu de crise depuis au moins cinq mois, et au total 15,7 % des patients avaient vu leur crise diminuer. Dans de nombreux cas, il n'y a plus eu de crise et on a constaté une nette amélioration physique, psychique et sociale. On n'a signalé que très peu d'effets secondaires et aucune intoxication. Le coût de la prise en charge par patient et par an s'est élevé à US $7 pour le phénobarbital sous forme générique et à US $8,4 pour la logistique.

Conclusion Le phénobarbital administré à faibles doses s'est révélé très efficace contre l'épilepsie. Toutefois, la mise en place de programmes visant à accroître le nombre de médecins en milieu rural et l'inclusion, au niveau national, du traitement anti-épileptique dans les activités des établissements de soins de santé s'imposent d'urgence ; au niveau international un programme de lutte contre l'épilepsie assurant des soins gratuits devrait être instauré.

Resumen

Tratamiento con fenobarbital y vigilancia de pacientes epilépticos en zonas rurales de Malí

Objetivo Evaluar la eficacia del fenobarbital como tratamiento de los enfermos de epilepsia en el Malí rural.

Métodos Se trató a domicilio a pacientes epilépticos con dosis diarias de fenobarbital que iban de 50 mg en los niños a 200 mg en los adultos, vigilándose la evolución de los pacientes. Tanto los enfermos como sus familias y las autoridades de las aldeas fueron asesorados respecto a la conveniencia de observar el tratamiento. Se aseguró el suministro ininterrumpido de fenobarbital genérico, y un médico rural hizo dos visitas de seguimiento a cada aldea para cerciorarse de que se estuvieran tomando las dosis correctas del fármaco. El médico facilitaba información a la población, distribuía el fenobarbital en cantidades suficientes para el intervalo entre las visitas y vigilaba la respuesta de los pacientes al tratamiento. Durante el primer año el médico visitó a los pacientes cada dos meses, y posteriormente cada cuatro meses.

Resultados En los seis meses previos al tratamiento la tasa promedio de crisis convulsivas entre los pacientes superó las cuatro por mes. Después de un año de tratamiento, el 80,2% de los pacientes no presentaron ninguna crisis convulsiva por espacio de al menos cinco meses. En total un 15,7% de los pacientes experimentaron una disminución de los ataques. En muchos casos las crisis convulsivas desaparecieron y la salud física, la salud mental y la posición social mejoraron. Se notificaron muy pocos casos de efectos secundarios, y ninguno de intoxicación. El costo del tratamiento por paciente y año fue de US$ 7 para el fenobarbital genérico y de US$ 8,4 para la logística.

Conclusión Las dosis bajas de fenobarbital fueron muy eficaces contra la epilepsia. Sin embargo, urge aplicar programas que incluyan a mayor número de médicos en las zonas rurales y, a nivel nacional, incluir el tratamiento de la epilepsia entre las actividades de los establecimientos de asistencia sanitaria. En el ámbito internacional, debe ponerse a punto un programa de lucha contra la epilepsia que proporcione tratamiento gratuito.

References

1. Gledhill RF. In the shadow of epilepsy. *Lancet* 1997;350:811.
2. Kale R. Bringing epilepsy out of the shadows. *BMJ* 1997;315:1-2.
3. *Bringing epilepsy out of the shadows. Launch of a global campaign*. Geneva: World Health Organization; 1997. Press release WHO/48.
4. Reynolds E. Out of the shadows. *New Scientist* 1997;27 September:48.
5. Senanayake N, Roman GC. Epidemiology of epilepsy in developing countries. *Bulletin of the World Health Organization* 1993;71:247-58.
6. Farnarier G, Moubeka-Mounguengui M, Kouna P, Assengone-Zeh Y, Gueye L. [Epilepsy in tropical developing countries: a study of selected health indicators.] *Epilepsies* 1996;8:189-213 (in French).
7. Jallon P. Epilepsy in developing countries. *Epilepsia* 1997;38:1143-51.
8. Farnarier G, Diop S, Coulibaly B, Arborio S, Dabo A, Diakite M, et al. [Onchocerciasis and epilepsy. An epidemiological study in Mali]. *Médicine tropicale* 2000;60:151-5 (in French).
9. Humbert A, Jaffré Y, Farnarier G. [An anthropological study of epilepsy in Mali: II – study in a hospital and in an urban setting.] *Epilepsies* 2001;13:33-8 (in French).
10. Arborio S, Jaffré Y, Farnarier G, Doumbo O, Dozon JP. [A study of kirikirimasien (epilepsy) in Mali: etiological and nosographic dimensions.] *Médicine tropicale* 1999;59:176-80 (in French).
11. Jaffré Y, Humbert A, Arborio S, Farnarier G. [An anthropological study of epilepsy in Mali: I – State of the art.] *Epilepsies,* 2001;13:29-32 (in French).
12. Farnarier G, Diop S, Coulibaly B, Traoré S, Dabo A, Diakité M, et al. [The epilepsy-onchocerciasis project (EOPM) in Mali. Epidemiological, clinical and biological aspects. Preliminary results.] *Bulletin de la Société de Pathologie Exotique* 2000;93: 264-5. (Summary of *Third Tropical Neurology Congress, Fort-de-France, Martinique, 30 November to 2 December 1998*) (in French).
13. Farnarier G, Vaz T, Diop S, Doumbo O. [Epilepsy risk factors in Mali. An epidemiological study in an area of endemic onchocerciasis.] *Epilepsies* 1999;11:222 Summary of *Journées Françaises de l'Epilepsie, Paris, 23–26 October 1999* (in French).
14. Gastaut H, Osuntokun BO. Proposals on antiepileptic pharmacotherapy for use in developing countries. *Epilepsia* 1976;17:355-60.
15. Osuntokun BO. Treatment of epilepsy: with special reference to developing countries. *Progress in Neuropsychopharmacology* 1979;3:81-94.
16. Shorvon SD, Farmer PJ. Epilepsy in developing countries: review of epidemiological, sociocultural and treatment aspects. *Epilepsia* 1988; 29 Suppl 1:S36-54.
17. Meinardi H. Why phenobarbital? *Epicadec News* 1993;1(February):7-8.
18. Pal DK, Das T, Chaudhury G, Johnson AL, Neville BG. Randomised controlled trial to assess acceptability of phenobarbital for childhood epilepsy in rural India. *Lancet* 1998;351:19-23.
19. Pal DK, Neville BG, Chaudhury G, Das T, Johnson AL. Antiepileptic drugs in developing countries. *Lancet* 1998;351:1210-1.
20. Trevathan E, Medina MT, Madrid A. Antiepileptic drugs in developing countries. *Lancet* 1998;351:1210-1.
21. Kaiser C, Asaba G, Mugisa C, Kipp W, Kasoro S, Rubaale T, et al. Antiepileptic drug treatment in rural Africa : involving the community. *Tropical doctor* 1998;28:73-7.
22. [All the world's countries]. *Population et Sociétés* July–August 2001; No. 370 (in French).
23. *Price indicator*. International Dispensary Association: Amsterdam; May 2001. Ref. IDA Co 253600.