Acta neurol. belg., 2006, **106**, 111-116

Guidelines

Guidelines for the management of epilepsy in the elderly

M. Ossemann, E. Bruls, V. de Borchgrave, C. De Cock, C. Delcourt, V. Delvaux, C. Depondt, M. de Tourchaninoff, T. Grisar, B. Legros, F. Liénard, I. Lievens, B. Sadzot and K. van Rijckevorsel

Groupe de travail des Centres francophones de référence de l'épilepsie réfractaire

Abstract

Seizures starting in patients over 60 years old are frequent. Diagnosis is sometimes difficult and frequently under- or overrated. Cerebrovascular disorders are the main cause of a first seizure. Because of more frequent comorbidities, physiologic changes, and a higher sensitivity to drugs, treatment has some specificity in elderly people.

The aim of this paper is to present the result of a consensus meeting held in October 2004 by a Belgian French-speaking group of epileptologists and to propose guidelines for the management and the treatment of epilepsy in elderly people.

Key words : Epilepsy ; elderly ; management.

Introduction

In industrialized countries, the population is ageing and therefore, the number of old patients with brain insults is increasing. Among these, seizures become a frequent and expensive medical problem. Due to physiologic changes of metabolism and higher frequency of comorbidities, diagnosis and treatment of epilepsy in elderly people need specific considerations.

This paper presents a consensus of the Belgian French-speaking group of the reference centres for refractory epilepsy on the management and the therapeutic attitude on epilepsy in elderly people.

Epidemiology

Elderly people have the highest incidence of new-onset seizures (Hauser *et al.* 1993). Twenty-four percent of new onset seizures happen after the age of 60 years old (Sander *et al.* 1990). This incidence seems to be due to the increasing lifespan and the increasing abilities of physicians to diagnose seizure in old people. Recent studies seems to show that the recurrence rate after a new-onset seizure in the elderly could be greater than 90% if untreated (Ramsay *et al.* 2004).

Diagnosis

The diagnosis of seizures is more difficult to establish because of the high incidence of co-diseases and "great imitators" of epilepsy in old age. These great imitators are the main cause of over diagnosis of epilepsy ; they are mainly syncope, episodic vertigo, hypoglycaemia, metabolic disorders, transient ischemic attacks, non-specific episodes of dizziness, confusional states, transient global amnesia or psychiatric illness.

On the other hand, focal seizures may remain ignored and be a cause of underdiagnosis of epilepsy. Symptoms as confusional states, hallucinations or automatisms are misleading and frequently considered as manifestations of neurodegenerative or psychiatric disorders. This is particularly emphasised by the predominance of focal seizures (52%) after 60 years in the Rochester epidemiological study (Hauser *et al.* 1993).

As with younger patients, EEG plays an important role, but is too often overestimated in elderly : normal variant patterns considered as epileptiform abnormalities, or non-specific abnormalities are more frequently recorded in older age (Drury and Beydoun 1993). Furthermore, variations of vigilance during EEG recording are more frequent and increase the complexity of the interpretation (Santamaria and Chiappa 1987). On the other hand, interictal epileptiform activities were recorded less often (26-37%) compared to younger patients (Dam *et al.* 1985, Henny *et al.* 1990, Drury and Beydoun 1998).

Therefore, this larger range of non specific data in older people decreases EEG sensitivity in this population. Consequently, prolonged EEG with sleep (night or nap) is often useful. We propose to do a sleep or a nap EEG recording if the awake EEG is negative.

Another specific indication for EEG recording in elderly patients, even in emergency conditions, is the suspicion of non convulsive status epilepticus when the patient is confused without known aetiology as metabolic disorder.

Aetiology

In elderly people, symptomatic focal epilepsies are the most represented and a presumed aetiology can be identified at least 70% of the cases. The most frequent causes of epilepsies in elderly people are cerebrovascular diseases (40.7%) and degenerative disorders (16.5%). Tumours (5.5%), traumatism (2.2%), metabolic complications, drug-induced seizures and infection are quite rare (Hauser *et al.* 1993). Moreover very rare cases of idiopathic generalized epilepsy (IGE) occurring after 60 years of age were reported (Loiseau *et al.* 1998, Hiyoshi and Yagi 2000). Gastaut considered that an onset of primary IGE is quite unusual in the elderly people and that earlier seizures are frequently found (Gastaut 1981). He also showed that most cases of late onset primary IGE occur in 40 to 50-year-old-women, stressing the role of menopause and sexual hormones on convulsive threshold (Gastaut 1982). Others have shown an increasing rate of seizure between 40 and 60 years of age.

Cerebrovascular disorders are the most common pathological factor underlying seizure(s) in elderly people (Sung and Chu 1989, Loiseau *et al.* 1990, Hauser *et al.* 1993) and the first cause of status epilepticus in this population (Sung and Chu 1989). Poststroke seizures are usually occur in a bimodal distribution : early onset (during the first two weeks after the stroke) and late onset seizures (Louis and McDowell 1967, Kilpatrick *et al.* 1992, Berges *et al.* 2000). The remote seizure rate in the acute poststroke period reaches 6% (Reith *et al.* 1997, Arboix *et al.* 1997) with a recurrence rate of 3-5.7% during the first year after the stroke and between 7.4-11.5% at five years (So *et al.* 1996, Burn *et al.* 1997). The cumulative incidence of late onset seizure was evaluated to 19% at 6 years (So *et al.* 1996). Retrospective studies have shown that the recurrence rate of late-onset seizures was around 35% (Gupta *et al.* 1988, Milandre *et al.* 1992, Kilpatrick *et al.* 1992). Some neuroimaging features seem to indicate risk of relapsing seizures. These features are : cortical involvement, large infarction, involvement of temporo-parietal cortex and hemorrhagic strokes (review in Ossemann 2002).

A recent study showed that the occurrence of one late-onset seizure significantly increases the risk of having a subsequent stroke. Thus, if no cause is found after a first seizure in a old patients, it is suggested that screening and treatment for vascular risk factor should be done (Cleary *et al.* 2004).

In a group of 81 patients with neuropathological signs of Alzheimer's disease, 10% had seizures and 10% had myoclonus (Hauser *et al.* 1986). A diagnosis of Alzheimer's disease or other dementia is associated with at least a six-fold increased risk of unprovoked seizure (Hesdorffer *et al.* 1996).

Treatment

Guidelines for treatment

When a seizure has been proved of epileptic origin, the first question is whether the seizure was provoked, therefore considered as an acute symptomatic seizure. Usually these symptomatic seizures do not require any chronic antiepileptic drug therapy.

If the first seizure appears unprovoked, the second question is : "what is the risk of relapse and should this seizure be treated ?".

There is no clear answer in the literature. In a prospective epidemiological study, seizure recurrence rates were 14, 29 and 34% at 1, 3 and 5 years after the first seizure. But in symptomatic seizure, depending on clinical features, this risk is increased to 20 to 80% at 5 years (Hauser *et al.* 1990). A remote cerebral lesion and epileptiform discharges on EEG are clear risk factors of recurrence after a first seizure (Rocca *et al.* 1987, Hauser *et al.* 1990, van Donselaar *et al.* 1991, FIRST Group 1993). Different studies have shown that seizure recurrence is more frequent in elderly patients (FIRST Group 1993, Ramsay *et al.* 2004).

Unfortunately, there is no agreement about the recurrence of seizure after treatment. A study has not shown any difference in the relapse rate with or without treatment (Hauser *et al.* 1990), even when in FIRST study treated patients have a lower recurrence rate of seizure (FIRST Group 1993).

Due to the high recurrence rate, we propose to treat after a first unprovoked seizure in the presence of a brain lesion or epileptiform abnormalities. For a first unprovoked seizure of unknown origin, the decision to treat should be individualised, after the evaluation of the vital risk induced by cormorbidities, the increased risk of status epilepticus in elderly population, the risk of serious injuries especially bone fracture in osteoporotic patients, and the potential adverse events of antiepileptic drugs (Fig. 1).

Choice of treatment

Guidelines for the choice of treatment in elderly persons with epilepsy are the same as for the whole epileptic population in general (de Borchgrave *et al.* 2002). However, specific consideration must be taken into account because elderly people present a hypersensitivity to antiepileptic drug (AED) (Table 1). The ideal drug in elderly patient does not exist. Ideally, this drug should be effective, well tolerated, with a simple metabolism and without significant drug interaction. The choice of an AED is difficult because there are few evidence based data on the use of these drugs in elderly patients, especially in the very old and in elderly with co-disease(s).

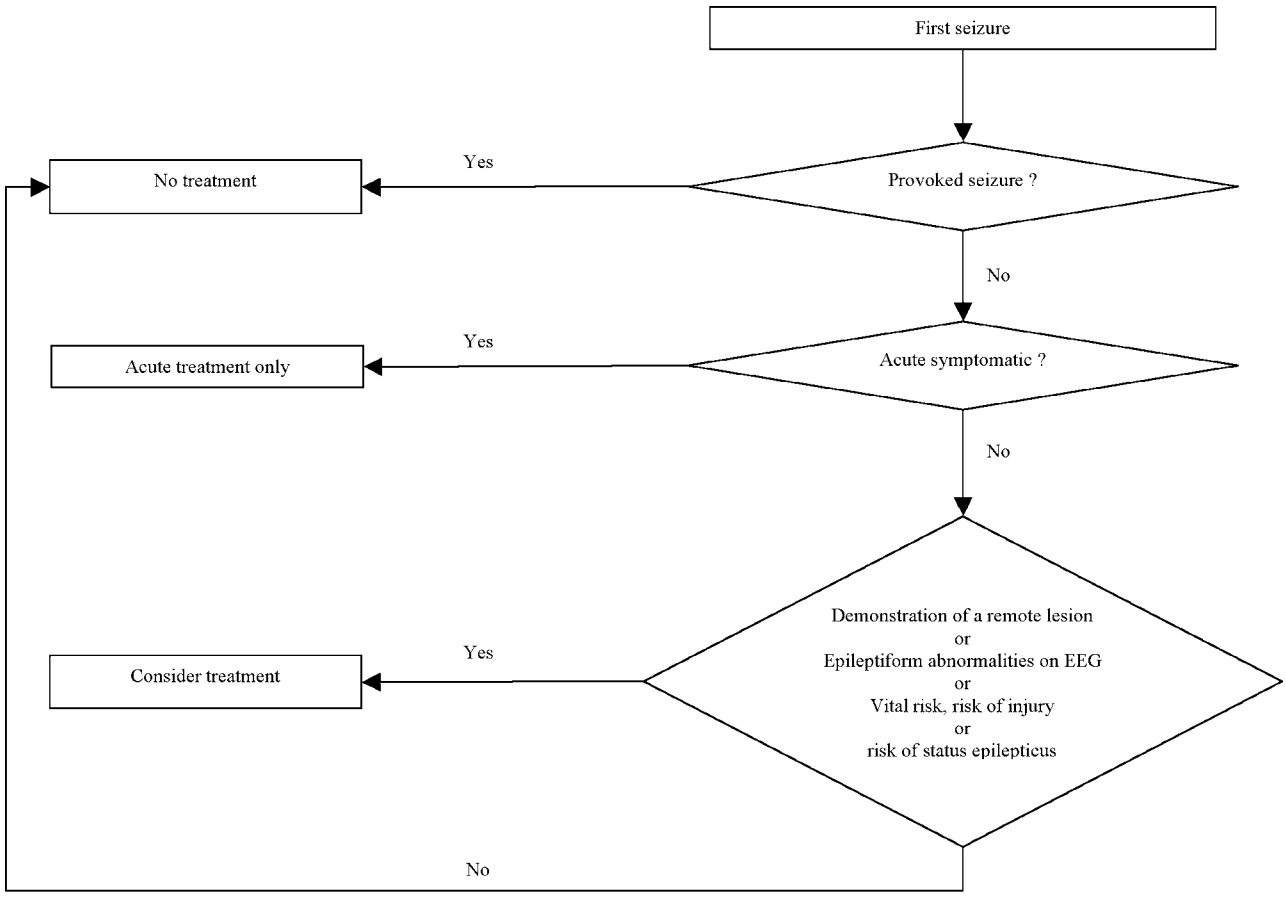


FIG. 1. — Algorithm for decision to treat after a first seizure

Table 1

Responsible factors of hypersensitivity to AED in elderly patients

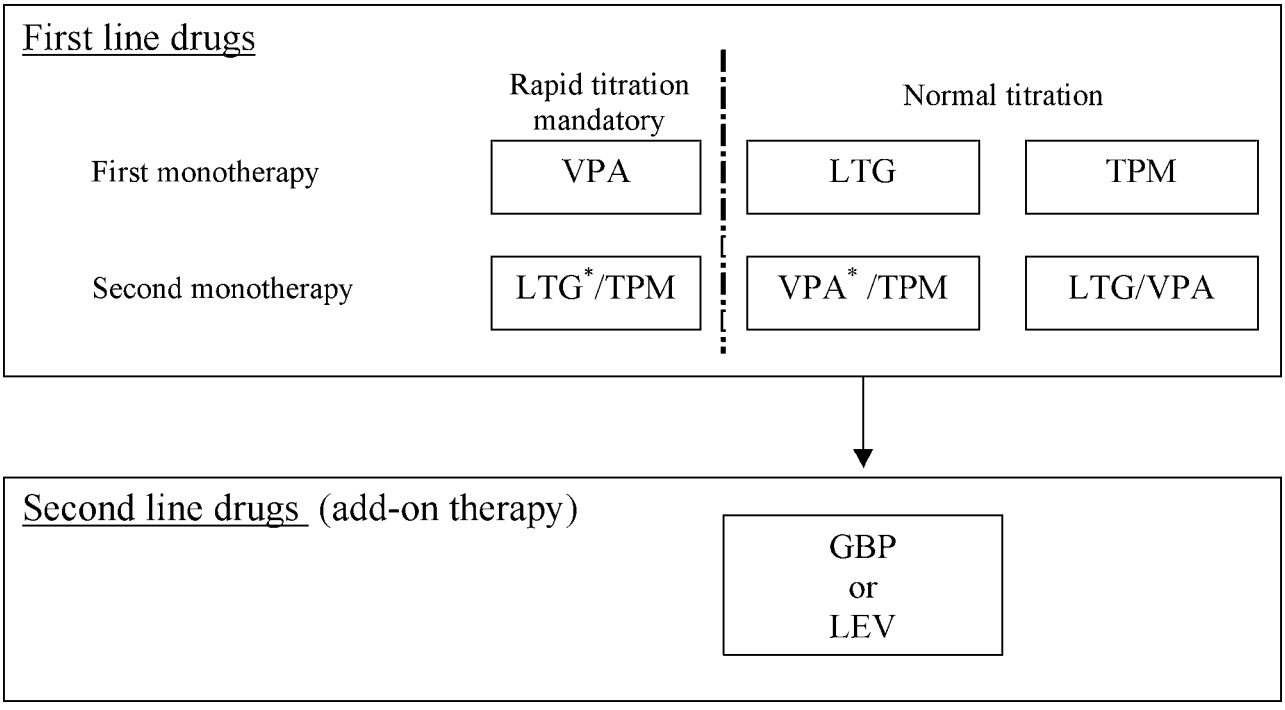
	Pharmacodynamic hypersensitivity	↓ Glomerular filtration rate	↓ Metabolic clearance	↓ Serum albumin (increase of free fraction)	≠body fat/lean mass ratio (↑ volume of distribution)	AEDs interaction
CBZ	+	–	+	–	+	↓ LTG, OXC, PB, PHT, TGB, TPM, VPA
GBP	+	+	–	–	+	–
LEV	+	+	–	–	+	–
LTG	+	–	+	–	+	(↑ CBZ)
OXC	+	–	+	–	+	↓ CBZ, (↑ PB), ↑ PHT
PB	+	+	–	–	+	↓ LTG, CBZ, OXC, PHT, TGB, TPM, VPA
PHT	+	–	+	+	+	↓ LTG, CBZ, OXC, PB, TGB, TPM, VPA
PGB	+	+	–	–	+	–
TGB	+	–	+	+	+	–
TPM	+	+	–	–	+	(↑ PHT)
VPA	+	–	+	+	+	↑ LTG, ↑ PB, (↑ CBZ, ↑ PHT)
VGB	+	+	–	–	+	–

CBZ : carbamazepine ; GBP : gabapentin ; LTG : lamotrigine ; OXC : oxcarbazepine ; PB : phenobarbital ; PHT : phenytoin ; PGB : pregabalin ; TGB : tiagabine ; TPM : topiramate, VPA : valproate ; VGB : vigabatrin.

Because pharmacodynamic and pharmacokinetic sensitivity in elderly patients is highly variable, there are no specific doses for these patients. Thus, the dosage must be adapted individually. The first general rule is “start low and go slow” ; the second one is monotherapy, as long as possible. Despite these principles, active searching of potential side effects is necessary.

Old AEDs have complex pharmacokinetic (phenytoin), important cognitive side effects (phenobarbitone), osteoporotic effects (phenobarbitone, phenytoin) (Christiansen *et al.* 1973), or important hepatic induction (carbamazepine, phenobarbitone, phenytoin). They should be avoided as much as possible in elderly patients. If treatment with phenytoin or phenobarbitone is mandatory, active search of osteoporosis by osteodensitometry should be done and in osteopenic patients treatment with calcium supplementation and vitamin D should be introduced, according to our previous guidelines on this subject (Legros *et al.* 2003).

In first line treatment and due to the adverse events of previously described old AEDs we recommend the use of valproate if a rapid titration or an intravenous use is necessary. This choice is justified because the Cochrane Review does not find any evidence of a significant difference exists between phenytoin and valproate for the outcome (Tudur *et al.* 2001). When urgent use of an AED is not mandatory, new AEDs may be proposed in accordance to the US guidelines on the use of new AEDs in new onset epilepsy (French *et al.* 2004) and the Belgian reimboursing rules. In a double-blind, multicenter study in elderly patients, the efficacy of lamotrigine has been shown equal to carbamazepine, but due to adverse events the rate of withdrawal is significantly higher with carbamazepine (Brodie *et al.* 1999). These results were recently confirmed by the US veteran study (Rowan *et al.* 2005). Topiramate is another first line alternative treatment. The result of a recent topiramate monotherapy prospective study had shown a high retention rate and a good tolerance to the drug in an elderly patients subgroup (Groselj *et al.* 2005). There is also some evidence for the usefulness of gabapentin and levetiracetam in elderly people, but the Belgian reimbursement rules limited there use in add-on therapy. Concerning gabapentin, a double-blind study shows a better tolerance than carbamazepine in old patients (Chadwick *et al.* 1998). These results were confirmed in the US veteran study (Rowan *et al.* 2005). Moreover in term of efficacy, no difference, was noted between gabapentin, carbamazepine and lamotrigine. Recent data concerning the use of levetiracetam in old patients revealed a favourable profile of tolerance (Cramer *et al.* 2003). The good efficacy of levetiracetam was shown in a subset analysis of the open-label add-on therapy KEEPER trial (Ferrendelli *et al.* 2003) and in a small first line therapy in elderly patients (Alsaadi *et al.* 2004) (Fig. 2).



GBP : gabapentin ; LTG : lamotrigine ; LEV : levetiracetam ; TPM : topiramate, VPA : valproate
*careful switch between LTG and VPA.

FIG. 2. — Choice of antiepileptic drugs in elderly

Despite preliminary study on a small group of elderly patients (Kutluay *et al.* 2003), the use of oxcarbazepine is more controversial in old people because an elevated risk of significant hyponatraemia (< 125 mmol/l). When used in elderly people, a careful evaluation of sodium level should be done, especially if oxcarbazepine is associated with diuretics, NSAIDs or carbamazepine and in the presence hyponatraemia related symptoms (Schmidt *et al.* 2001)

Up to now, there is no assessment on the efficacy and the tolerance of pregabalin and tiagabine in old people.

Conclusion

Epileptic seizures are common in elderly people. They are frequently under- or over-diagnosed. An extensive diagnostic work-up is sometimes necessary to rule out "imitators of epilepsy" and to confirm the epileptic origin of the seizure. Due to the predominance of cerebrovascular aetiology in this population, a screening for cardio-vascular risk factors should be proposed when there is no evident cause to the seizure.

Unlike in the younger, a first unprovoked seizure should be more often treated. The decision to start a treatment must take into account the balance between advantages and side effects of the drug. The used drug must preferably be well tolerated without important drug interactions. The treatment should be administrated slowly and at the lowest necessary dosage. Despite these precautionary measures, surveillance of potential side effects remains necessary.

REFERENCES

HAUSER W. A., ANNEGERS J. F., KURLAND L. T. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota : 1935-1984. *Epilepsia*, 1993, **34** : 453-468.

SANDER J. W., HART Y. M., JOHNSON A. L., SHORVON S. D. National General Practice Study of Epilepsy : newly diagnosed epileptic seizures in a general population. *Lancet*, 1990, **336** : 1267-1271.

RAMSAY R. E., ROWAN A. J., PRYOR F. M. Special considerations in treating the elderly patient with epilepsy. *Neurology*, 2004, **62** : 24S-29.

DRURY I., BEYDOUN A. Pitfalls of EEG interpretation in epilepsy. *Neurol. Clin.*, 1993, **11** : 857-881.

SANTAMARIA J., CHIAPPA K. H. The EEG of drowsiness in normal adults. *J. Clin. Neurophysiol.*, 1987, **4** : 327-382.

DAM A. M., FUGLSANG-FREDERIKSEN A., SVARRE-OLSEN U., DAM M. Late-onset epilepsy : etiologies, types of seizure, and value of clinical investigation, EEG, and computerized tomography scan. *Epilepsia*, 1985, **26** : 227-231.

HENNY C., DESPLAND P. A., REGLI F. Première crise épileptique après l'âge de 60 ans : étiologie, présentation clinique et EEG. *Schweiz. Med. Wochenschr.*, 1990, **120** : 787-792.

DRURY I., BEYDOUN A. Interictal epileptiform activity in elderly patients with epilepsy. *Electroencephalogr. Clin. Neurophysiol.*, 1998, **106** : 369-373.

LOISEAU J., CRESPEL A., PICOT M. C., DUCHE B., AYRIVIE N. *et al.* Idiopathic generalized epilepsy of late onset. *Seizure*, 1998, **7** : 485-487.

HIYOSHI T., YAGI K. Epilepsy in the elderly. *Epilepsia*, 2000, **41 Suppl 9** : 31-35.

GASTAUT H. [Individualization of so-called benign and functional epilepsy at different ages. Appraisal of variations corresponding the predisposition for epilepsy at these ages]. *Rev. Electroencephalogr. Neurophysiol. Clin*, 1981, **11** : 346-366.

GASTAUT H. "Benign" or "functional" (versus "organic") epilepsies in different stages of life : an analysis of the correpsonding age-related variations in the predisposition to epilepsy. In : *Henri Gastaut and the Marseilles school's contribution to the neurosciences* (EEG Suppl. No 35). BROUGHTON R. J. (ed.). Amsterdam : Elsevier Biomedical Press, 1982, 17-44.

SUNG C. Y., CHU N. S. Status epilepticus in the elderly : etiology, seizure type and outcome. *Acta Neurol. Scand.*, 1989, **80** : 51-56.

LOISEAU J., LOISEAU P., DUCHE B., GUYOT M., DARTIGUES J. F. *et al.* A survey of epileptic disorders in southwest France : seizures in elderly patients. *Ann. Neurol.*, 1990, **27** : 232-237.

BERGES S., MOULIN T., BERGER E., TATU L., SABLOT D. *et al.* Seizures and epilepsy following strokes : recurrence factors. *Eur. Neurol.*, 2000, **43** : 3-8.

LOUIS S., MCDOWELL F. Epileptic seizures in nonembolic cerebral infarction. *Arch. Neurol.*, 1967, **17** : 414-418.

KILPATRICK C. J., DAVIS S. M., HOPPER J. L., ROSSITER S. C. Early seizures after acute stroke. Risk of late seizures. *Arch. Neurol.*, 1992, **49** : 509-511.

ARBOIX A., GARCIA-EROLES L., MASSONS J. B., OLIVERES M., COMES E. Predictive factors of early seizures after acute cerebrovascular disease. *Stroke*, 1997, **28** : 1590-1594.

REITH J., JORGENSEN H. S., NAKAYAMA H., RAASCHOU H. O., OLSEN T. S. Seizures in acute stroke : predictors and prognostic significance. The Copenhagen Stroke Study. *Stroke*, 1997, **28** : 1585-1589.

BURN J., DENNIS M., BAMFORD J., SANDERCOCK P., WADE D. *et al.* Epileptic seizures after a first stroke : the Oxfordshire Community Stroke Project. *BMJ*, 1997, **315** : 1582-1587.

SO E. L., ANNEGERS J. F., HAUSER W. A., O'BRIEN P. C., WHISNANT J. P. Population-based study of seizure disorders after cerebral infarction. *Neurology*, 1996, **46** : 350-355.

SO E. L., ANNEGERS J. F., HAUSER W. A., O'BRIEN P. C., WHISNANT J. P. Population-based study of seizure disorders after cerebral infarction. *Neurology*, 1996, **46** : 350-355.

GUPTA S. R., NAHEEDY M. H., ELIAS D., RUBINO F. A. Postinfarction seizures. A clinical study. *Stroke*, 1988, **19** : 1477-1481.

KILPATRICK C. J., DAVIS S. M., HOPPER J. L., ROSSITER S. C. Early seizures after acute stroke. Risk of late seizures. *Arch. Neurol.*, 1992, **49** : 509-511.

MILANDRE L., BROCA P., SAMBUC R., KHALIL R. Les crises épilepstiques au cours at au décours des accidents cérébrovasculaires. Analyse clinique de 78 cas. *Rev. Neurol. (Paris)*, 1992, **148** : 767-772.

OSSEMANN M. Crises épileptiques et épilepsies d'origine vasculaire : caractéristiques cliniques, électroencéphalographiques et scannographiques. *Rev. Neurol. (Paris)*, 2002, **158** : 256-259.

CLEARY P., SHORVON S., TALLIS R. Late-onset seizures as a predictor of subsequent stroke. *Lancet*, 2004, **363** : 1184-1186.

HAUSER W. A., MORRIS M. L., HESTON L. L., ANDERSON V. E. Seizures and myoclonus in patients with Alzheimer's disease. *Neurology*, 1986, **36** : 1226-1230.

HESDORFFER D. C., HAUSER W. A., ANNEGERS J. F., KOKMEN E., ROCCA W. A. Dementia and adult-onset unprovoked seizures. *Neurology*, 1996, **46** : 727-730.

HAUSER W. A., RICH S. S., ANNEGERS J. F., ANDERSON V. E. Seizure recurrence after a 1st unprovoked seizure : an extended follow-up. *Neurology*, 1990, **40** : 1163-1170.

ROCCA W. A., SHARBROUGH F. W., HAUSER W. A., ANNEGERS J. F., SCHOENBERG B. S. Risk factors for complex partial seizures : a population-based case-control study. *Ann. Neurol.*, 1987, **21** : 22-31.

HAUSER W. A., RICH S. S., ANNEGERS J. F., ANDERSON V. E. Seizure recurrence after a 1st unprovoked seizure : an extended follow-up. *Neurology*, 1990, **40** : 1163-1170.

VAN DONSELAAR C. A., GEERTS A. T., SCHIMSHEIMER R. J. Idiopathic first seizure in adult life : who should be treated ? *BMJ*, 1991, **302** : 620-623.

FIRST GROUP. Randomized clinical trial on the efficacy of antiepileptic drugs in reducing the risk of relapse after a first unprovoked tonic-clonic seizure. First Seizure Trial Group (FIR.S.T. Group). *Neurology*, 1993, **43** : 478-483.

DE BORCHGRAVE V., DELVAUX V., DE TOURCHANINOFF M., DUBRU J. M., GHARIANI S. *et al.* Therapeutic strategies in the choice of antiepileptic drugs. *Acta Neurol. Belg.*, 2002, **102** : 6-10.

CHRISTIANSEN C., RODBRO P., LUND M. Incidence of anticonvulsant osteomalacia and effect of vitamin D : controlled therapeutic trial. *Br. Med. J.*, 1973, **4** : 695-701.

LEGROS B., BOTTIN P., DE B., V, DELCOURT C., DE TOURTCHANINOFF M. *et al.* Therapeutic issues in women with epilepsy. *Acta Neurol Belg.*, 2003, **103** : 135-139.

TUDUR S. C., MARSON A. G., WILLIAMSON P. R. Phenytoin versus valproate monotherapy for partial onset seizures and generalized onset tonic-clonic seizures. *Cochrane. Database. Syst. Rev.*, 2001,CD001769.

FRENCH J. A., KANNER A. M., BAUTISTA J., ABOU-KHALIL B., BROWNE T. *et al.* Efficacy and tolerability of the new antiepileptic drugs I : treatment of new onset epilepsy : report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*, 2004, **62** : 1252-1260.

BRODIE M. J., OVERSTALL P. W., GIORGI L. Multicentre, double-blind, randomised comparison between lamotrigine and carbamazepine in elderly patients with newly diagnosed epilepsy. The UK Lamotrigine Elderly Study Group. *Epilepsy Res.*, 1999, **37** : 81-87.

ROWAN A. J., RAMSAY R. E., COLLINS J. F., PRYOR F., BOARDMAN K. D. *et al.* New onset geriatric epilepsy : a randomized study of gabapentin, lamotrigine, and carbamazepine. *Neurology*, 2005, **64** : 1868-1873.

GROSELJ J., GUERRINI R., VAN OENE J., LAHAYE M., SCHREINER A. *et al.* Experience with topiramate monotherapy in elderly patients with recent-onset epilepsy. *Acta Neurologica Scandinavica*, 2005, **112** : 144-150.

CHADWICK D. W., ANHUT H., GREINER M. J., ALEXANDER J., MURRAY G. H. *et al.* A double-blind trial of gabapentin monotherapy for newly diagnosed partial seizures. International Gabapentin Monotherapy Study Group 945-77. *Neurology*, 1998, **51** : 1282-1288.

CRAMER J. A., LEPPIK I. E., RUE K. D., EDRICH P., KRAMER G. Tolerability of levetiracetam in elderly patients with CNS disorders. *Epilepsy Research*, 2003, **56** : 135-145.

FERRENDELLI J. A., FRENCH J., LEPPIK I., MORRELL M. J., HERBEUVAL A. *et al.* Use of levetiracetam in a population of patients aged 65 years and older : a subset analysis of the KEEPER trial. *Epilepsy & Behavior*, 2003, **4** : 702-709.

ALSAADI T. M., KOOPMANS S. U. Z. A., APPERSON M. I. C. H., FARIAS S. A. R. A. Levetiracetam monotherapy for elderly patients with epilepsy. *Seizure*, 2004, **13** : 58-60.

KUTLUAY E., MCCAGUE K., D'SOUZA J., BEYDOUN A. Safety and tolerability of oxcarbazepine in elderly patients with epilepsy. *Epilepsy Behav.*, 2003, **4** : 175-180.

SCHMIDT D., ARROYO S., BAULAC M., DAM M., DULAC O. *et al.* Recommendations on the clinical use of oxcarbazepine in the treatment of epilepsy : a consensus view. *Acta Neurol. Scand.*, 2001, **104** : 167-170.

Dr. M. OSSEMANN,
Service de neurologie,
Cliniques Universitaires UCL de Mont-Godinne,
Avenue Gaston Thérasse 1,
B-5530 Yvoir (Belgium).
E-mail : ossemann@nchm.ucl.ac.be.