

THÉRAPEUTIQUE

Les antiépileptiques thymorégulateurs dans le traitement des symptômes comportementaux et psychologiques de la démence (SCPD)

Anticonvulsant mood stabilizers in the treatment of behavioral and psychological symptoms of dementia (BPSD)

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MOTS CLÉS

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Résumé Les démences, outre les troubles cognitifs prédominants qui les définissent, sont associées à des perturbations du comportement dont le retentissement est à différents niveaux un facteur déterminant dans la prise en charge de ces patients. Le traitement de ces symptômes psychocomportementaux est essentiel et s'il n'existe à l'heure actuelle pas de solution thérapeutique satisfaisante pour ces troubles, il est nécessaire de chercher une alternative aux neuroleptiques usuellement employés, qui posent de réels problèmes de tolérance dans cette population âgée. Les antiépileptiques, dont certains ont montré une activité thymorégulatrice, font depuis quelques années l'objet de recherches dans cette indication. Cette revue de la littérature a pour objectif d'évaluer l'intérêt et les limites des antiépileptiques thymorégulateurs (carbamazépine, acide valproïque, gabapentine, lamotrigine, topiramate, oxcarbazépine) dans le traitement des symptômes dits « non cognitifs » de la démence.

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KEYWORDS

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Mood stabilizers

Summary

Introduction. – Dementia, besides the dominant cognitive disorders that define it, is associated with behavioral disturbances, the consequences of which are, on various levels, a determining factor for the handling of these patients. The treatment of behavioral and psychological symptoms is essential and although, to date, no therapeutic solution is satisfactory, it is necessary to look for an alternative to the neuroleptics usually employed, which raise real problems of tolerance in this geriatric population.

Background. – For several years, anticonvulsants, among which some have shown mood stabilizing activity, have been the object of research in this indication. The purpose of this review of the literature is to assess the interest and the limits of anticonvulsant mood stabilizers (carbamazepine, valproic acid, gabapentin, lamotrigine, topiramate, oxcarbazepine) in the treatment of the so-called “noncognitive” symptoms of dementia. Their mechanism of action in mood disorders is not well known, but it would appear to be via the modulation of glutamate-mediated excitatory synaptic transmission and gamma-aminobutyric acid (GABA)-mediated inhibitory synaptic transmission that anticonvulsants might reduce behavioral symptoms in demented patients.

Methods. – The method employed in this work was a systematic bibliographic review, in which only the double-blind placebo-controlled studies or the clinically detailed enough open-labelled studies using validated scales were retained.

Results. – Among these medications, only carbamazepine demonstrated its efficacy in behavioral and psychological symptoms of dementia (BPSD) in controlled studies, notably that of Tariot et al. [J Am Geriatr Soc 42 (1994) 1160–1166 and Am J Psychiatry 155 (1998) 54–61] and Olin et al. [Am J Geriatr Psychiatry 9 (2001) 400–405], but with significant adverse events (sedation, hyponatremia, cardiac toxicity), particularly in the elderly and, being a strong enzymatic inducer, with a high likelihood of drug–drug interactions. Valproic acid showed some interesting results in BPSD within a large number of open studies and case reports. However, among the five controlled studies that have been published [Curr Ther Res 62 (2001) 51–67; Am J Geriatr Psychiatry 9 (2001) 58–66; Int J Geriatr Psychiatry 17 (2002) 579–585; Curr Alzheimer Res 2 (2005) 553–558 and Am J Geriatr Psychiatry 13 (2005) 942–945], none confirmed its efficacy on these symptoms. Regarding its tolerability in the geriatric population, no notable major side effect was reported (haematologic and hepatic effects are not more frequent than in the general population), except possible excessive sedation. Moreover, it appears that valproic acid could have neuroprotective effects, even if the contrary has been observed in a recent study. More studies need to be (and are being) conducted, notably on the interest of valproic acid in prophylaxis of BPSD. Gabapentin seems to be worthwhile and well tolerated in this indication, but no controlled study has been conducted to prove its efficacy, even if a quite important number of case reports and open studies have shown encouraging results. Concerning lamotrigine, which may potentially induce severe cutaneous side effects when administered with valproic acid, this drug has shown its efficacy in bipolar disorders and two recent case reports seem to indicate some interest in BPSD. Furthermore, lamotrigine appears to have neuroprotective effects. Although topiramate has shown interesting results in one open study in BPSD, its use in demented patients cannot be recommended because of its deleterious effect on cognitive functions. Oxcarbazepine, theoretically, could be an alternative to carbamazepine, which is, as aforesaid, the only anticonvulsant that proved its interest in BPSD. However, no clinical study has yet been published to support this hypothesis. This drug is better tolerated than carbamazepine, but induces severe and more frequent hyponatremia.

Discussion and conclusion. – Finally, although we all know that antipsychotics should no longer be prescribed in the elderly, the treatment of behavioral and psychological symptoms of dementia remains a difficult problem, considering the lack of a real alternative to these medications. Anticonvulsant mood stabilizers are an interesting solution but none of them, other than carbamazepine, which did, but which is not better tolerated than the usual drugs in this population – was able to prove its efficacy in this indication. Among these medications, valproic acid, gabapentin and lamotrigine should be studied further, and the neuroprotective effect of some of them is an interesting route for research.

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