Lamotrigine as a treatment of agitation in Dementia

Background:
- Psychomotor agitation is common in patients with dementia but there are no well-established or evidenced-based effective treatments.
- Non-pharmacological interventions remain the mainstay of treatment but are not always feasible or sufficient.
- Antipsychotics are the most commonly used drugs but concerns regarding tolerability limit their use.
- Anticonvulsants are receiving growing attention due to their better safety profile.

Objective:
We report a case of a patient with dementia and behavioral disturbance treated with lamotrigine, and make a brief review of the literature of anticonvulsants use in the treatment of agitation and aggression in dementia.

Methods:
Retrospective review of the clinical chart and literature review on the topic.

Clinical case
- A 69 years-old woman with behavioral variant Frontotemporal Dementia, severe stage, totally dependent on activities of daily living and with severe speech difficulties, developed progressive aggressive behavior.
- In the following 6 months, quetiapine until 200mg/daily and then risperidone until 1mg/daily was tried, with no success.
- Lamotrigine was then introduced and titrated until 100mg/daily.
- Since this dosage and in the 2 next consultations, no more aggressive behavior were observed.

Literature Review

The majority of studies have focused on two anticonvulsants: carbamazepine and valproate.

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<tr>
<th>Anticonvulsant</th>
<th>Description</th>
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<td>Carbamazepine</td>
<td>The most evidence-based supported, but concerns regarding tolerability, not well established long term use efficacy and safety and, its enzyme inducing effect limit its use [1]</td>
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<td>Oxcarbazepine</td>
<td>Negative results in a placebo-controlled study and higher risks of hyponatremia make it not suitable [2]</td>
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<td>Valproic Acid</td>
<td>Currently not recommended due to lack of efficacy, with a 2009 Cochrane review concluding that this drug is ineffective in treating agitation and with an unacceptable rate of adverse effects. Some authors pointed that open trials and extension studies of controlled trials are positive and some of the controlled studies included show limitations, such as small numbers of patients included samples or low dosages used</td>
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<td>Lamotrigine</td>
<td>Shares many cellular mechanisms of action with Carbamazepine and Valproate, making it a drug of keen interest. Acts blocking voltage-dependent sodium and calcium channels and reducing glutamate release. Antiepileptic drugs, as a class, have been associated with impairment of cognitive function although to varying degrees, lamotrigine either had a neutral effect or improved cognitive functioning. [3] Review of the available literature also suggests that lamotrigine is effective and well tolerated in elderly patients with epilepsy and bipolar disorder [4]. A 2014 open-label trial with lamotrigine observed a decrease on the Neuropsychiatric Inventory (NPI) agitation subscale and in the diazepam equivalent dose, concluding that lamotrigine may be effective in severe dementia and may avoid increasing the dosage of antipsychotic drugs. [5]</td>
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Conclusion:
With this case we describe the potential use of lamotrigine in severe dementia to manage agitation and as an alternative to conventional treatment, with a well-established safety profile in the elderly population. Randomized clinical trials are necessary to confirm these data.

References: