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## Treatment of apathy in Alzheimer's disease with transdermal rivastigmine: report of three cases

### *Tratamento da apatia na doença de Alzheimer com rivastigmina transdérmica: relato de três casos*

Dear Editor,

Apathy in Alzheimer's disease is one of the most difficult behavioral and psychological symptoms to treat. Anticholinesterasic drugs, dopaminergic agonists, and psychostimulants are treatment alternatives based on studies with contradictory results.<sup>1</sup> The use of transdermal rivastigmine has not been sufficiently studied in clinical trials, especially regarding the treatment of apathy. We report below 3 cases of dementia and apathy treated with transdermal rivastigmine, with behavioral symptoms analysis, cognitive testing and outcome measurement in the first, second, third and sixth months.

Case reports: Three female patients were evaluated – MO (81 years old), ECN (74 years old) and DM (84 years old) – all of them meeting the criteria for Alzheimer's Disease (based on DSM-IV) and for apathy (based on the following criteria proposed by Robert P, 2009:<sup>2</sup> 1) the core feature of apathy, diminished motivation, must be present for at least four weeks; 2) two of the three dimensions of apathy (reduced goal-directed behaviour, goal-directed cognitive activity, and emotions) must also be present; 3) there should be identifiable functional impairments attributable to apathy; 4) exclusion criteria are specified to exclude symptoms

and states that mimic apathy. After the diagnosis of Alzheimer's disease, the patients were treated with transdermal rivastigmine (4.6mg in the first month and 9.5mg after the second month). The improvement of apathy was observed after the introductions of anticholinesterasic treatment. The three cases are presented below:

1) DM presented at first meeting with: Mini Mental State Examination (MMSE) of 15/30, poor verbal contact, walking impairment, loss of manual abilities, and social isolation. After two months of treatment, the patient started to interact during the examination, returned to her manual and social activities, improved her walking balance and presented a MMSE of 21/30. After six months, the improvements were maintained.

2) ECN presented at first meeting with: MMSE of 20/30, difficulties in verbal contact, loss of instrumental activities of daily living (iADL), and social isolation. After two months of treatment, the patient returned with great improvement in verbal contact, returned to her iADL and presented a MMSE of 22/30. After six months, the improvements were maintained.

3) MO presented at first meeting with: MMSE of 13/30, poor verbal contact, loss of iADL and interruption of her morning exercise (walking). After two months of treatment, the patient was more collaborative, showed iADL improvement, returned to her physical activity and presented an MMSE of 10/30. The improvements were maintained after 6 months.

Discussion: Apathy is the most common neuropsychiatric syndrome in Alzheimer's disease, affecting 30 to 60% of patients.<sup>1,2</sup> Its pharmacologic therapy is based on three strategies: psychostimulants, dopaminergic agonists and anticholinesterasic drugs.<sup>1</sup>

Despite being first tested and developed for the improvement of cognition in Alzheimer's disease, anticholinesterasic drugs showed many benefits in the treatment of behavioral and psychological symptoms related to dementia, including apathy. Although systematic reviews point to a lack of well-designed studies concerning this issue, anticholinesterasic drugs remain as an appropriate therapy for apathy.<sup>3,4</sup> The new presentation of transdermal rivastigmine has been studied as an option with fewer adverse effects (nausea and vomiting) when compared to other oral anticholinesterasic drugs,<sup>5</sup> but no studies concerning their use in behavioral symptoms have been conducted. In the cases reported above, there was a surprising improvement in the apathy of all patients, regardless of the changes in cognitive function. This finding brings new perspectives for the conduction of future randomized and double-blind studies evaluating the use of transdermal rivastigmine.

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## Disclosures

Writing group member	Employment	Research grant <sup>1</sup>	Other research grant or medical continuous education <sup>2</sup>	Speaker's honoraria	Ownership interest	Consultant/ Advisory board	Other <sup>3</sup>
Alessandra Lamas Granero	Geriatric Clinic – São Paulo Commerce Workers Union	-	-	-	-	-	-
Giancarlo Lucchetti	Geriatric Clinic – São Paulo Commerce Workers Union	-	-	-	-	-	-

\* Modest

\*\* Significant

\*\*\* Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.

For more information, see Instructions for authors.

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## Use of lithium during pregnancy: a case report using clinical decision analysis

### Utilização de lítio durante a gravidez: um relato de caso usando análise de decisão clínica

Dear Editor,

There is great potential for the application of decision-making analysis in Psychiatry; especially in situations where the risk of continuing treatment is considerable. While the implementation of decision analysis can be time consuming,

once in place, it can be a useful tool in difficult clinical situations.<sup>1,2</sup>

Case: A 32-year-old Hispanic female with a 9-year-history of bipolar disorder type I, presenting 4 severe manic episodes, requiring prolonged hospitalizations. The patient was stabilized with 1500mg of lithium carbonate per day with a normal serum level. The patient wanted to become pregnant. She had questions whether to continue lithium and having the risk of having a child with Ebstein's or another anomaly, or to discontinue the treatment and face the risk of relapse. The patient and the psychiatrist decided to use a decision tree for the potential outcomes, which are measured from 0, being the least desirable condition, "patient relapses and has an abnormal child", to 10, being the best option "patient does not relapse, and has a normal child". The patient and the psychiatrist came to a mutual decision to assign utilities based on their therapeutic relationship and the patient knowing that 10 is having a normal child and 0 having a child with a heart abnormality. Numbers in between were based on outcomes subjectively assigned by the patient with the help of her psychiatrist. Figure 1 illustrates the construction of the decision tree. The probabilities are assigned to each event taken from reports from literature. The sum of the probabilities of the events represented in each chance node must equal 1. Based on what the literature has described, approximately 21% of women who are pregnant decide to continue lithium treatment.<sup>3</sup> The risk of Ebstein's anomaly has been described to be approximately 0.05%. Studies have reported that in patients taking lithium, the risk for developing abnormalities is approximately 11%; for presenting a cardiac abnormality it is close to 8%, and for Ebstein's anomaly it is approximately 2%.<sup>4,5</sup> Pregnant women with bipolar disorder have a 52% probability of experiencing recurrence of their illness during their pregnancy if lithium is discontinued. Additionally, a patient receiving lithium treatment will have a 37% likelihood of relapsing.<sup>6</sup> Patients who stopped lithium may have a 55% risk of relapse within 3 months of discontinuation of treatment.<sup>5</sup> Based on these probabilities, the calculations were made from far right to left and where placed in each chance node. The patient decided that