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B12, Folate and Homocysteine levels monitoring in Clinical Psychiatry

Ioannis Christopoulos* and Evangelos Neroutsos

Address: Psychiatry Department, Thriassion General Hospital, Elefsina, Greece
* Corresponding author

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Background

Valproic acid (VLA), carbamazepine (CBZ) and most of the newest anti-seizure agents have nowadays an established use in psychiatric pharmacotherapy, not only in bipolar affective disorder but also,off-license though in a variety of disorders. The effects of the anti-seizure medications on B12, folate and homocysteine levels have been a topic of research. The related 1-carbon metabolism has been implicated in mental disorders. So, taking into account all the above we reviewed the literature about the potential benefit of monitoring B12 and folate levels on patients receiving anti-seizure medication, especially VLA or CBZ.

Materials and methods

We reviewed the guidelines as given by official Institutes in UK and USA, namely NICE (National Institute for Clinical Excellence) and APA (American Psychiatric Association). Articles related to the subject were also reviewed after relevant search via the Medline [1,2]. As far as the involvement of impaired 1-carbon metabolism in the neurochemistry of affective and anxiety disorders, it appears the evidence from both clinical (involving trials albeit of a small scale) and basic research, is suggestive of a degree of involvement in their pathophysiology (stronger evidence exists for folate). We also found evidence suggestive of adverse effects of the anti-seizure medications on B12, folate and homocysteine levels-none of which is routinely monitored (or advised so by guidelines) in patients receiving such medication for mental disorders.

Results

As far as the involvement of impaired 1-carbon metabolism in the neurochemistry of affective and anxiety disorders, it appears the evidence from both clinical (involving trials albeit of a small scale) and basic research, is suggestive of a degree of involvement in their pathophysiology (stronger evidence exists for folate). We also found evidence suggestive of adverse effects of the anti-seizure medications on B12, folate and homocysteine levels-none of which is routinely monitored (or advised so by guidelines) in patients receiving such medication for mental disorders.

Conclusions

The findings both from clinical studies and basic science research suggest a role of the an impaired 1-carbon metabolism in the pathophysiology of cognitive decline (including Alzheimer's disease) and mood disorders, especially depression with implications regarding treatment. There are also weaker indications of involvement in anxiety disorders. In brief, B12, folate and homocysteine are involved in very important central nervous system functions: Folate metabolism is linked to biopterin-dependent neurotransmitter synthesis and biogenic amine methylation with B12 involved as a co-factor. Homocysteine and its metabolite homocysteic acid, may have a direct neurotoxic effect, involving NMDA receptors. Homocysteine levels are increased in B12 and folate deficiency. It appears that the long term use of anti-seizure drugs, especially carbamazepine and valproate has unfavorable effects on B12 and folate levels. Taking all the above into consideration, we find it reasonable to suggest that a six monthly or

yearly monitoring of B12, folate and possibly homocysteine levels would be a cost effective intervention with advantageous effects in this group of patients.

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