The effect of adjunctive nutraceuticals in bipolar disorder: A systematic review of randomized placebo-controlled trials

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OBJECTIVE

To summarize all randomized placebo-controlled trials evaluating the efficacy of nutraceuticals as an add-on therapy in bipolar disorder (BD).

METHODS

We performed a systematic search following the PRISMA guidelines, from inception to February 2019. We included all original articles written in English which met the following criteria:

- (1) Participants: individuals with **bipolar disorder (type I or type II), mania or schizoaffective disorder, bipolar type**, diagnosed by a clinician according to international valid diagnostic criteria (i.e. DSM or ICD).
- (2) Intervention: **nutraceuticals** of any type, dosage and form of administration (i.e. omega 3 fatty acids, vitamins, minerals, amino acids, N-acetyl cysteine, probiotics, etc), in combination with standard care.
- (3) Comparison: **placebo plus standard care**.
- (4) Outcomes: **depressive symptoms or manic symptoms**, evaluated through standardized measures, clinical global impression, functioning, adverse events, other outcomes.
- (5) Study design: **randomized controlled trials, both parallel and crossover**.

The PRISMA flow chart of the study selection process has been reported in Figure 1.

RESULTS

After identifying 6584 potentially relevant publications, we finally included **25 studies**, testing the following nutraceuticals:

- **Fatty acids (6)**
- **Micronutrients (7)**
- **Amino acids (7)**
- **Probiotics (1)**
- **Combination of different nutraceuticals (4)**

Even if some compounds have shown **promising results (i.e. fatty acids and N-acetyl cysteine for depression, amino acid drinks and folic acid for mania)**, the majority of nutraceuticals did not cause significant improvements in comparison to placebo. We could not perform a meta-analysis due to the high **heterogeneity of trials**, which were also affected by some **methodological caveats**.

The **risk of bias** of the included studies has been reported in Figure 2.

CONCLUSION

The present systematic review revealed **inconsistent results about the effectiveness of nutraceuticals on symptoms of BD**. Some of them seem to be potentially useful, but significant results often rely on single or few studies. However, **nutraceuticals appeared generally safe and free of important side effects**.

More clinical trials are needed to better elucidate the role of nutraceuticals in treating core symptoms of BD. It is important for future researchers to **better characterize and, possibly, harmonize the samples recruited** in trials examining the role of nutraceuticals in BD. Additionally, all concomitant conditions potentially influencing the response to treatment (i.e, baseline nutrient levels, dietary regimen) should be clearly explained.

Finally, **the role of promising substances not included in this review (e.g. saffron, curcumin, etc.) should be tested** by researchers in future investigations.

Full reference

Fusar-Poli, L., Surace, T., Vanella, A., Meo, V., Patania, F., Furnari, R., Signorelli M.S., Aguglia, E. (2019). The effect of adjunctive nutraceuticals in bipolar disorder: A systematic review of randomized placebo-controlled trials. *Journal of Affective Disorders*, 252, 334–349. doi:10.1016/j.jad.2019.04.039