Rapid response to Methylphenidate as an add-on therapy to mirtazapine in the treatment of major depressive disorder in terminally ill cancer patients: A four-week, randomized, double-blinded, placebo controlled study.

Reference: Ng Chong Guan, Marco PM Boks, Kit CB Roes, Nor Zuraida Zainal, Ahmad Hatim Sulaiman, Tan Seng Beng, Niek J de Wit. European Neuropsychopharmacology 2014; 24: 491-8.

Abstract

Background: This is a 4 week, randomized, double-blind, placebo-controlled study to examine the effects of methylphenidate as add-on therapy to mirtazapine compared to placebo for treatment of depression in terminally ill cancer patients.

Methods: It involved 88 terminally ill cancer patients from University of Malaya Medical Centre, Kuala Lumpur, Malaysia.

- sberg Depression Rating Scale (MADRS) score from baseline to day 3 was analyzed by linear regression. Changes of MADRS and Clinical Global Impression-Severity Scale (CGI-S) over 28 days were analyzed using mixed model repeated measures (MMRM). Secondary analysis of MADRS response rates, defined as 50% or more reduction from baseline score.

Results: A significantly larger reduction - sberg Depression Rating Scale (MADRS) score in the methylphenidate group was observed from day 3 (B=4.14; 95% CI=1.83–6.45). Response rate (defined as 50% or more reduction from baseline MADRS score) in the methylphenidate treated group was superior from day 14. Improvement in Clinical Global Impression-Severity Scale (CGI- S) was greater in the methylphenidate treated group from day 3 until day 28. The drop-out rates were 52.3% in the methylphenidate group and 59.1% in the placebo group (relative risk=0.86, 95%CI=0.54–1.37) due to cancer progression. Nervous system adverse events were more common in methylphenidate treated subjects (20.5% vs 9.1%, p=0.13).

Conclusion: In conclusions, methylphenidate as add on therapy to mirtazapine demonstrated an earlier antidepressant response in terminally ill cancer patients, although at an increased risk of the nervous system side effects.

Strengths:
Randomized, double-blinded, placebo controlled
Multiple outcome measurements with same assessment tool over 28d period
Baseline characteristics same in both groups

Weaknesses:
High drop out rates for both groups (due to cancer progression, adverse events, withdrawn)
? clinically relevant considered limited lifespan
Diagnosis of depression confounded by cancer fatigue, lack of concentration, weight loss, decreased appetite
Social supports not explored
Needed 120 pts to power the study

Relevance to palliative care: Terminally ill patients experience a lot of distress and psychological suffering due to physical symptoms and poor prognosis. Conventional antidepressants are hampered by slow response rate. Need to consider risk/benefit for each patient on an individual basis, considering social supports and adverse events.