Assessment of the Efficacy of Immediate Release Methylphenidate, Sustained Release Methylphenidate, and Modafinil for Patients with Primary Brain Tumor

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Introduction

Impaired neurocognitive function (NCF) is common in primary brain tumor (PBT) patients and may reflect the effects of tumor burden and treatment. NCF is an important aspect of quality of life (QOL). Impaired NCF has been associated with diminished QOL. Treatment of neurocognitive decline frequently involves the use of psychostimulants such as methylphenidate, d–three-methylphenyl HCL, dextroamphetamine, and pemoline. Mechanism of action of psychostimulants includes counteracting the effects of disease x treatment x patient factors on the monoamine pathways in the frontal brainstem system (including the RAS) (Iversen, 1975; Simon et al., 1980). Psychostimulants have been reported to reduce fatigue and depression (consistent with monoamine hypothesis of depression) among cancer patients (Breitbart & Mermelstein, 1992; Burns & Eisendrath, 1994; Fernandez et al., 1986,1987; Olin & Masand, 1996; Weiztner et al., 1995).

However, limited research is available regarding the efficacy of immediate release methylphenidate (IRM) in treating NCF and QOL impairment among PBT patients. It was expected that patients receiving methylphenidate would demonstrate differential effects of tumor burden on longitudinal analyses of mood, fatigue, and QOL improvements in NCF and neurobehavioral function among PBT patients. Evidence for improvement in QOL is equivocal.

There is a lack of research assessing the efficacy of sustained release methylphenidate (SRM) and other stimulants such as the novel vigilance enhancing drug modafinil in treating impaired NCF among PBT patients. The objective of this trial was to compare IRM with SRM and modafinil for the improvement of NCF of PBT patients. It was expected that patients receiving methylphenidate would demonstrate differential improvement on tests of memory, executive function and psychomotor processing speed relative to patients treated with modafinil, while patients receiving modafinil would exhibit differential improvement on tests of attention measures.

Methods

We conducted a two arm, open-label, pilot study comparing the efficacy of IRM, SRM, and modafinil as treatment of NCF dysfunction and fatigue among PBT patients. Twenty-four PBT patients were identified by their treating neuro-oncologist if they were considering treatment with a psychostimulant. Patients were randomly assigned to each of the three groups: IRM (ritalin), SRM (concerta), and modafinil (provigil).

Patients received ritalin 10 mg, concerta 18 mg, or modafinil 200 mg for 4 weeks (mean duration = 33 days). Assessment of NCF and QOL was performed before and after 4 weeks of stimulant therapy.

Statistical Analyses: Pre-treatment versus post-treatment changes in the NCF performance were analyzed using standardized scores. Raw/standardized scores were used for fatigue, symptom, and QOL measures. The likelihood ratio statistic, controlling for baseline performance and adjustment for multiple comparisons, was used to measure longitudinal changes in NCF. The practice effect adjusted reliable change index (RCI/Pe) was also calculated for NCF measures and was used to determine the frequency of “clinically significant” change.

Discussion

TMTB showed substantial clinical improvement (36% patients improved) upon stimulant treatment. Particularly, those in IRM group showed remarkable post-treatment gains on TMTB.

No other substantial clinical changes were noticeable.

Longitudinal analyses comparing methylphenidate with modafinil showed that patients receiving methylphenidate (slope = 2.017) demonstrated greater statistical improvement than patients receiving modafinil (slope=0.975) on TMTB (chi-square statistic (df = 1) = 10.272, p < 0.001).

There were no statistically significant changes on longitudinal analyses of mood, fatigue, and QOL measures.

Overall, methylphenidate improved psychomotor processing speed but did not result in differential change on memory or executive function measures.

Modafinil did not demonstrate differential effects on measures of attention.