

Original Article

Methylphenidate Rehabilitation Effect in Severe Head Injury

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ABSTRACT

Background: Annually, millions of people are affected by traumatic brain injuries which cause long - lasting sequels such as cognitive or motor system dysfunctions. Methylphenidate, a neurostimulant drug, has been proposed as a therapeutic agent in brain injuries. Unlike previous reports, new studies have shown more benefits from its use in traumatic brain injuries. This clinical trial was going to define the value of methylphenidate use in the treatment of traumatic brain injuries.

Methods: A double blind, randomized clinical trial was implemented. 60 patients, hospitalized in Intensive Care Units, were randomly put into treatment and control groups. In the treatment group, methylphenidate was administered 5 mg daily, from day 5 to 9 of their hospitalization and 10 mg daily thereafter. Normal Saline was administered as placebo to control patients. All the patients were followed by monitoring these parameters: vital signs, Glasgow Coma Scale (GCS) and brain function. Physicians, who were responsible for patients' monitoring, did not know patients' status of drug reception (drug or placebo).

Results: During the first day GCS in the treated group was 5.43 ± 1.52 and in the control patients was 5.37 ± 1.30 ($P = 0.87$). After 14 days, GCS was 14 ± 0.66 and 10.37 ± 2.13 in treated and control patients, respectively ($P < 0.05$).

Conclusion: This study confirmed the results of similar recent studies done during the past 5 years. They found improved brain functions using methylphenidate in traumatic brain injuries.

Key words: Methylphenidate, brain functions, brain trauma

Millions of people around the world suffer brain damage due to trauma every year¹ and the treatment expenses of severe head trauma is about \$160,000 per case annually². Similar to physical disabilities and organic dysfunction, cerebral dysfunction and cognitive disorders which remain for months and years after accidents are important subjects in neurosurgery.³ Supportive care in ICU is not the only purpose for patients with head injury⁴, however, use of different cerebral stimulant drugs in rehabilitating patients with head injury within the last decade has received much confirmation^{5,6}.

Methylphenidate is a cerebral stimulant which has been used to improve memory and cognitive disorders and motor responses following head trauma⁷. However different studies on short term and long term prognosis of the use of

methylphenidate in clinical and animal models showed some discrepancies⁸⁻¹⁰. In some studies it was confirmed that the use of methylphenidate as an effective drug may be useful in head injury rehabilitation. Although some studies have found methylphenidate as an excellent effective drug in cerebral function restoration and increasing the level of memory to the optimal state¹¹, a lot of other studies could not find any significant differences between this drug and placebos¹⁰⁻¹². Nevertheless methylphenidate is nowadays used widely in USA¹³.

In this study the level of consciousness and function of patients who were given methylphenidate during their hospitalization and two months later were assessed and compared to the control group.

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Materials and Methods

Sixty injured patients with GCS < 9 and no history of HTN on admission were chosen and randomly divided into treatment and control groups.

Following basic data of patients were recorded: GCS, nervous signs, vital signs and cerebral function condition. Cases in the treatment group received a single dose of 5 mg methylphenidate via gastric tube at 8 am for the first two days. From the third day, the dosage increased to 5 mg q12h. Vital signs, cerebral function, level of consciousness, GCS and presence of seizure were recorded by neurosurgery assistants who were not aware of the patient's group. Cerebral function was assessed by an assistant at the end of the first and second month.

Data were presented as mean \pm SD. Mann Whitney U test was used to compare the mean values of GCS between the two groups. Friedman test was used to compare GCS scores before and after the intervention. Frequency data were compared between the two groups using chi-square test. Data were finally analyzed in SPSS 9.0.

Results

Mean age of patients in the treatment and control groups were 31 ± 8.7 and 31 ± 6.7 ($P = 0.94$) respectively. 50% of cases in the treatment group were female versus 40% in the control group ($P = 0.43$). No patients developed seizure, sudden elevation of blood pressure or heart rate. Mean GCS values for both groups during this study were presented in table 1. At the end of the second month 86.7% of cases in the treatment group had

Table 1. Comparison of GCS between treatment and control groups during the study. Data are mean \pm SD

Day	Treatment group (n=30)	Control group (n=30)
1	5.43 \pm 1.52	5.37 \pm 1.30
7	8.77 \pm 1.57	7.73 \pm 1.84
8	10.9 \pm 1.75*	7.93 \pm 1.89
9	12.10 \pm 1.24*	8.33 \pm 1.97
10	13.13 \pm 1.36*	9.4 \pm 2.08
14	14 \pm 0.66*	10.37 \pm 2.13
30	14.66 \pm 0.03*	11.67 \pm 2.38
60	14.81 \pm 0.1*	12.33 \pm 1.75

* $P < 0.05$ compared to the value in control group.

optimal cerebral function while only 3.3% of patients in the control group showed optimal cerebral function ($P = 0.000$). Hemiparesia and paraparesia were 10% in the treatment group and 33.3% in the control group ($P < 0.05$). GCS scores were increased in both groups during the course of study ($P < 0.05$).

Discussion

In order to assess the effect of methylphenidate on improvement of cerebral function, level of consciousness and motor responses in patients with severe head injury, a randomized double blind clinical trial was carried out. Results of the study showed significant improvement of cerebral function in the treatment group though William et al¹⁰ could not find any differences between methylphenidate and placebos on the improvement of cerebral function in children with head injury. Laboratory study on rats showed reasonable improvement of brain function after methylphenidate administration⁹.

In Kelin Date's survey, the prescription of 15 mg methylphenidate caused reasonable improvement of cognition and cerebral function during rehabilitation period¹¹.

Wroblewski et al¹⁴ showed that prescription of methylphenidate caused acceptable improvement of cognition and cerebral function and nervous signs in their case group rather than in their control group. Speech et al¹² could not find any significant effects of methylphenidate use in patients with head injury.

Recent studies have shown better effects of methylphenidate to eliminate cerebral dysfunction due to head injury compared to studies done in early 1990s.

It seems that greater sample size and more refinement of disturbing factors put effective influence on these results. Since the majority of patients had multiple traumas many factors may confound the final conclusion on the effect of this drug. Another concern for the routine use of methylphenidate is its cost.

Probable seizure followed by the use of methylphenidate should not be the reason to quit the use of methylphenidate. Ruplexy's survey did not prove increased incidence of seizure following the use of methylphenidate in head injured patients¹⁴.

Now with respect to the acceptable improvement of cerebral function in patients with head injury using methylphenidate and absence of serious complications, it can be suggested that the use of methylphenidate in patients with head injury after

the 5th day without the history of hypertension can decrease rehabilitation period and accelerate restoration of cerebral function to the optimal level.

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