

METHYLPHENIDATE IN STROKE PATIENTS WITH DEPRESSION¹

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ABSTRACT Johnson ML, Roberts MD, Ross AR, Witten CM: Methylphenidate in stroke patients with depression. *Am J Phys Med Rehabil* 1992;71:239-241.

The treatment of depression after stroke is a difficult clinical problem. Many of the medications used to treat patients with depression in the general population have significant potential side effects that are of particular concern in elderly patients. We reviewed the records of ten patients with stroke treated with methylphenidate for depression during an inpatient rehabilitation program. Improvement was noted in seven patients. This suggests that methylphenidate in the treatment of post-stroke depression merits further study.

KEY WORDS: Stroke, Depression, Methylphenidate, Rehabilitation

Untreated depression has been termed a major unmet need of stroke survivors. The depression may frequently interfere with a patient's ability to participate in the rehabilitation program. Depression can further affect the interpersonal relationships already altered by the impairment resulting from the stroke.

Methylphenidate, at present approved for use only in the treatment of attention-deficit disorders, has been used in the treatment of depression in elderly patients as an alternative to tricyclic or other antidepressant medications. In particular, methylphenidate has been reported to be of use in the treatment of post-stroke depression.

This report summarizes our experience with the use of methylphenidate in the treatment of post-stroke depression in patients in an inpatient rehabilitation setting.

METHODS

Ten patients who were admitted to our rehabilitation facility with a diagnosis of cerebrovascular accident (CVA) were placed on methylphenidate for treatment of post-stroke depression during the 9-month period from June 1989 through February 1990. The charts were reviewed for age, sex, race, psychosocial history, site of lesion and concurrent medical problems. All patients were seen by a psychologist on the treatment team for assessment of mental status and for supportive psychotherapy. The dose and duration of methylphenidate treat-

ment, the patient's response to treatment and side effects resulting from treatment were noted.

Case 1

A 74-yr-old white male was admitted to the rehabilitation hospital 3 wk after sustaining a CVA. On admission to the rehabilitation hospital the patient was noted to have right hemiplegia, a right hemisensory deficit and Broca's aphasia. The patient was oriented to person and place but not date. Short- and long-term memory impairment was noted. The patient's affect and mood were depressed. The impression of the treating psychologist was that the patient was suffering from an adjustment disorder with depressed mood.

Ten days into the patient's rehabilitation stay it was felt that the patient's depressed mood and poor mental concentration were hindering his rehabilitation progress. Treatment with methylphenidate (5 mg po daily) was begun. The next day he was noted to appear brighter during conversations. The members of the treatment team noted improvement in the patient's affect during the following week. His memory deficits and attention span were also noted to be improved. By the beginning of the 2nd wk of treatment he began to make excellent progress in all therapies. The methylphenidate was continued for 4 more wk and then discontinued. He was discharged a week later with no evidence of depression. No adverse effects of methylphenidate were noted during the course of treatment.

Case 2

A 65-yr-old white female was admitted to the rehabilitation hospital 5 wk after sustaining a right middle cerebral artery infarction. The patient's past medical history was significant for major depression. She had been intermittently treated with perphenazine-amitriptyline (2/10 mg po bid) for 10 yr and

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had undergone four electroconvulsive therapy treatments.

Physical examination on admission to the rehabilitation facility revealed left hemiparesis and dysarthria. Sensation was intact. On review of systems the patient stated that she was prone to crying episodes, and she felt that her depression and anxiety had intensified since her recent stroke. She admitted to insomnia, but denied fatigue or decrease in appetite, sexuality or concentration. The patient was not on antidepressant medication on admission. The impression of the treating psychologist was that the patient was suffering from a general anxiety disorder and recurrent major depression.

A psychiatrist was consulted regarding appropriate therapy for depression. Three weeks into her rehabilitation course she was started on a trial of methylphenidate (5 mg po bid) as recommended by the psychiatrist. The next day her sobbing episodes had decreased in frequency. Two days later she had no problems with sleep, and her motivation in therapies was noted to be improved. By discharge the following week, her sobbing episodes had greatly decreased in frequency, her lethargy and withdrawal had diminished, and she was no longer complaining of depression. There were no adverse side effects noted on the medication, and the patient was discharged on methylphenidate (5 mg po bid).

The remainder of the patient data is summarized in Table 1.

RESULTS

Over a period of 9 months ten patients with a diagnosis of CVA were treated with methylphenidate (Table 1). Six of the patients had sustained left hemispheric strokes. Eight of the patients had a diagnosis of adjustment disorder with depressed mood; one was diagnosed with major depression, and the other was diagnosed with a combination of major depression and an anxiety disorder. Eight of the ten patients were noted to have concomitant

attention deficits. All of the patients were noted to have cognitive deficits on initial evaluation, and in each case these deficits were felt to worsen with depression.

Seven of the ten patients showed clinical improvement after therapy with methylphenidate; four of them were discharged home on this medication.

The doses used ranged from 5 mg (qam) to 15 mg (bid), with the length of therapy ranging from 5 days to 1 month. The earliest manifestations of response to therapy were improvement in mood and improvement in attention span. Of interest is that each patient who was felt to improve with treatment was described as having an attention-deficit disorder. The response time ranged from 1 to 5 days. Of the three patients who did not respond to treatment, one was diagnosed with major depression and had a poor response to other antidepressant medications. One patient became agitated and verbally abusive with marked improvement of these symptoms when the medication was stopped. The increased agitation seen in that case and insomnia seen in two other cases were the only side effects observed.

DISCUSSION

Tricyclic antidepressants and similar compounds (bicyclics and tetracyclics), monoamine oxidase inhibitors and newer serotonin reuptake inhibitors are currently the mainstay in the treatment of depression. These medications, used for treatment of depression in the general population, can have significant side effects that may be worse in patients who already have cognitive impairment because of a stroke or are elderly with comorbidities. The possibility of significant medication side effects may explain why depression in stroke survivors is frequently untreated.

Electroconvulsive therapy has also been used for poststroke depression. In one series of 14 patients with stroke depression, 2 of 14 patients improved with this treatment. Despite the fact that an arrhyth-

TABLE 1
Summary of patient data

Patient Number	Age	Sex	Hemisphere of Stroke	Prior Psychiatric History	Response	Response Time	Methylphenidate Dose at Discharge
<i>yr</i>							
1	74	Male	Left	None	Improved	1	None
2	65	Female	Right	Major depression	Improved	1	5 mg bid
3	64	Female	Right	Alcohol abuse	Improved	1	None
4	66	Male	Right	None	Improved	3	5 mg qam
5	78	Female	Right	None	Improved	3	None
6	66	Female	Left	Major depression	No change		None
7	83	Male	Left	None	Agitation	3	None
8	75	Female	Left ^a	None	No significant improvement		None
9	76	Female	Left	None	Improved	4	5 mg qam
10	67	Female	Left	None	Improved	1	5 mg qam

^a Located in left brain stem.

mia developed in one of these patients, electroconvulsive therapy was felt to be a safe and effective alternative for poststroke depression.¹ However, other reports have described memory impairment as an additional complication of electroconvulsive therapy. In many patients with stroke, this may pose a particularly bothersome problem.

Several studies have investigated the use of psychostimulants in the treatment of elderly depressed patients in states of apathy defined as "lack of interest and emotional involvement in one's surroundings," and in patients described as rehabilitation failures secondary to poor cooperation and motivation.²⁻⁹ In a retrospective review of 25 patients with poststroke depression, 13 (52%) recovered completely from depression after treatment with methylphenidate. Mood usually improved within 48 h.⁸

Methylphenidate is a mild psychostimulant that is structurally related to amphetamine and has similar qualities. It has its effects centrally in the cortical and subcortical areas of the brain. It is postulated that methylphenidate heightens mood by affecting various neurotransmitter systems. Methylphenidate blocks the reuptake of serotonin and norepinephrine, and it has dopaminergic activity as well.¹⁰ Thus, it may affect post-stroke depression by correcting depletion of biogenic amines induced by stroke. Contraindications include hypersensitivity, motor tics, glaucoma or family history of Tourette's syndrome.

Side effects of methylphenidate include insomnia and nervousness (which can be controlled by decreasing the dose or omitting the drug in the afternoon and evening), hypersensitivity reactions, cardiac arrhythmia, hypertension and hypotension. Although methylphenidate should be used with caution in patients with a cardiac history, Kaufmann et al.⁴ described a rapid therapeutic response (24 to 48 h) with no adverse side effects in four depressed patients after cardiac surgery. There is some clinical evidence that methylphenidate may lower seizure threshold in patients either with prior history of seizures or with no prior history but with electroencephalogram abnormalities. Although two of our patients had history of seizure disorder and were on anticonvulsants, neither of them had clinical seizures while on the medication. Psychologic dependence is possible and therefore methylphenidate should be used cautiously in patients with a history of substance abuse (see package insert).

The drug is absorbed readily when using conventional oral tablets. Effects peak in ~2 h and persist for 3 to 6 h after a single dose.¹⁰ Brain concentrations exceeding those of plasma would account for more prominent central rather than peripheral effects. Methylphenidate may lead to increased plasma levels of imipramine, Dilantin, phenobarbital, desipramine and primidone and patients on these medications need to be carefully monitored.

With the exception of methylphenidate and elec-

troconvulsive therapy, most forms of therapy for post-stroke depression generally take from 2 to 3 wk to be effective. This can be of particular importance in the rehabilitation setting where the patient can be treated only for a limited amount of time.

The ease of administration, the speed of response and the relatively few side effects would make methylphenidate an attractive alternative for the treatment of post-stroke depression if it could be shown to be effective.

There are a number of limitations to this retrospective series. The number of cases reviewed was small, there were no controls and there were no systematic outcome measures used to collect quantitative data. In most cases methylphenidate was chosen because a quick response to therapy was desired, but doses were not uniform. Patients who were placed on other antidepressants were not always given adequate trials of those drugs, so no comments can be made regarding the success of methylphenidate in cases where other antidepressants failed. Also, all patients were concomitantly receiving supportive psychotherapy. However, in only one case was the methylphenidate treatment initiated <10 days after admission. In each case, the supportive psychotherapy alone was not felt to have improved the patient's mood sufficiently to enable full participation in therapy and maximum benefit for the rehabilitation program.

In summary, seven of our ten patients treated with methylphenidate showed clinical improvement. This suggests that methylphenidate is an important potential treatment of post-stroke depression and may be worth further study.

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