

CASE REPORT

Intravenous Valproate Therapy

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ABSTRACT

Four cases of acute manic episode (bipolar-I disorder), not responding to oral valproate or other mood stabilizer and neuroleptics were given injection valproate intravenously. Three out of 4 patients showed good response and tolerance to intravenous valproate.

Key words: Intravenous Valproate, Manic episode.

INTRODUCTION

Valproate has emerged as an efficacious medication in the management of acute manic episode and in the long-term maintenance therapy of bipolar mood disorder (Bowden et al., 1994; McElroy et al., 1996).

Injection valproate is now available for intravenous use. When valproate is administered intravenously, the peak plasma concentration is reached faster, the hepatic first-pass metabolism is bypassed and the gastrointestinal disturbances are less common (Devisky et al., 1995). Duggal et al, (2000) found intravenous valproate to be efficacious in a case of schizoaffective disorder.

The report summarizes the use of injection valproate administered intravenously in 4 cases of acute manic episode (bipolar-I disorder) (APA, 1994).

The following protocol (Grunze et al., 1999) was used in all the 4 patients for administration of intravenous valproate. Dosage of the drug was decided empirically as per the following protocol and it was not based on the body weight of the patients.

Each ml of injection valproate contains 100 mg of valproic acid. At a time 250 mg of injection valproate (2.5 ml) diluted in 250 ml of normal saline was given to the patient in the form of slow infusion drip over a period of 1 hour.

combination of valproate and clozapine.

She was hospitalised and started on intravenous valproate as per the protocol mentioned above. Oral valproate was stopped and clozapine 200 mg/day continued.

After the 1st infusion on day-1, on clinical assessment some improvement was observed in the patient's behaviour. On day 5 relatives reported that her manic symptoms had reduced substantially. By day 15 patients was in complete remission. At present she is maintained on 750 mg of oral valproate and 200 mg of clozapine.

CASE REPORT - 2

A 17 year old female patient, suffering from bipolar-I disorder since 18 months

Days	Form	Dose	Frequency
Day 1, 2, 3	Inj. valproate	250 mg TV	Once daily
Day 4, 5, 6	Inj. valproate	250 mg IV	Twice daily
Day 7 onward	Inj. valproate	250 mg IV	Thrice daily
Day 15 onward	Tab. valproate	250 mg orally	Thrice daily

* Injection Valproate was continued Day-7 onwards till the remission was achieved.

* Valproate was started from the day of remission or Day-15 onwards.

Blood pressure of the patients was monitored twice everyday during hospitalization, keeping in view the side effect of hypotension due to intravenous Valproate. Patients were also monitored for development of hypersensitivity to the drug.

CASE REPORT - 1

A 50 year old female patient, suffering from bipolar-I disorder since 20 years, maintained on lithium, presented with acute manic episode and symptoms of hypothyroidism low pulse rate, edema face and feet. So lithium was stopped and she was started on carbamazepine. As she did not tolerate carbamazepine, she was switched to oral valproate, which was gradually increased to 1750 mg per day over a period of 3 weeks. Clozapine 200 mg per day was added, since no significant improvement was noted with valproate alone. When she did not show any improvement with the

presented with acute manic episode. As she did not respond to a course of lithium and haloperidol combination over a period of 2 weeks) she was administered a course of 8 ECTs. Since this also was not very useful, tablet clozapine 200 mg per day was added. With this a substantial clinical improvement was observed. But on follow up visit, she complained of excessive sedation and incontinence of urine during sleep. Clozapine had to be reduced and stopped. But after stopping clozapine manic symptoms increased and so the patient was started on intravenous valproate as per the protocol mentioned above, in this patient also, after the 1st infusion on day-1, clinical assessment showed some improvement in patient's behavior. On day-5 a significant improvement in grandiosity was noted. By day- 15 she was in complete remission. During the therapy she complained of nausea and had one episode of vomiting. At present she is well maintained only on 750 mg of oral valproate.

CASE REPORT-3

A 52 year old male patient, suffering from bipolar-I disorder since 25 years, had 6 episodes of mania in 2001 and so was considered as rapid cyeler. He was tried on various combinations of lithium, clozapine, olanzapine, lorazepam, thioridazine and had received a course of 10 ECTs with little improvement. So he was considered for intravenous valproate therapy.

Like previous 2 patients, this patient also showed a substantial improvement in psychomotor agitation after the 1st infusion of valproate on day-1. By the 5th day a very significant improvement was observed clinically and almost complete remission was achieved by the day-9. At present patient is well maintained on 800 mg or oral valproate. This patient did not have any side-effects except minimal sedation.

CASE REPORT-4

A 16 year old female patient, suffering from bipolar-I disorder since 1 year was brought by her relatives with acute manic episode. She was treated with haloperidol, chlorpromazine, carbamazepine, oxcarbazepine, and a course of 6 ECTs over a period of 4 weeks. She had developed ataxia with carbamazepine and diplopia with

oxcarbazepine. As she did not show any substantial improvement clinically and had adverse reactions to the mood stabilisers, she was considered for intravenous valproate therapy.

Unlike the previous 3 patients, in this patient, no improvement in symptoms was observed after the infusion on day-1 and even on day-5 there was only a minimal improvement. On day-6 Patient developed giddiness, ataxia and incoordination and so the therapy was discontinued.

DISCUSSION

Intravenous valproate therapy for acute manic episode seems to be a very useful option. Though there are no formal guidelines or criteria, developed for the use of intravenous valproate, One may prefer to use it for the patients who do not respond to oral valproate, or other mood stabilizers and antipsychotic medications. The onset of improvement is almost immediate and a substantial improvement is noticed within 5 days of the treatment. Most of the patients seem to tolerate this therapy well, though some of them may have excessive sedation, nausea, vomiting or CNS side effects. While using this therapy, one needs to be careful as patients may develop hypotension or hypersensitivity reaction. The positive

clinical experience warrants a double-blind placebo controlled trial to confirm these findings.

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