Amineptine Dependence

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Amineptine, a substance containing an imipramine like tricyclic ring, is a psychotropic agent which has psychostimulant and anti- depressant properties[1,2]. Pharmacologically, it is known to increase release of dopaniine at the synapse and a reduction of dopamine uptake. Athighdoses, serotonin sup take is inhibited. This mode of actional the level of cerebral amines suggests the likelihood of original properties, in particular thymoanaleptic, possibly associated with stimulant activity. Two of our cases, from an open study, started consuming 1200-1400 mg of amineptine per day[3] (recommended dose 200400 mg). This study reports the follow-up of one of the cases from the previous study and another patient who developed dependence on amineptine.

Case 1

K.A., 50 years old, a non-functioning partner in a company had first psychotic episode at the age of 24 years. From 1971 onward he is being treated as a case of bipolar affective disorder. Forlast5years features of major depression along with feelings of 'as if controlled' have remained predominant and unchanged. He received multiple anti-depressants and two courses (5 each) of ECT without any respite. Amineptine was first added to the regimen in 1990 but was soon with drawns because of lack of improvement It was restarted in 1992. Anti-depressant activity was more produced this time. Within next five weeks he started to have the feelings of increased energy and joy which would last for about two hours followed by a period of misery. During this period his longstanding erectile impotence would improve though 2not good enough for intercourse. He would frequently masturbate. Gradually the duration of euphoria and well-being decreased and necessitated frequent and increasing doses. He himself would call it 'dependence' on the drug. The maximum number of tablets he took in 24 hours reached to twenty-six (2600 mg). The longest period of abstinence in last two years was during May and June of 1993 while on a trip to USA. Blood biochemistry had remained unremarkable. In February, 1994 he was admitted with acute psychotic episode after taking around 3,500 mg of amineptine in forty-eight hours, five days prior to admission. The psychotic features settled in four days but he continued to have strong urge for amineptine. Baseline biochemical investigations revealed mild leucocytosis. Liver function tests were unremailable.

Case 2

I.M., 41 year old pharmacist was admitted through emergency with five days history of irritability, disturbed sleep and depressed mood. A known case of major depressive disorder, he was put on amineptine in June, 1991. Within few weeks the dose escalated from two tablets to tenaday. In order to give it up he tried to substitute it with an amphetamine derivative. However, this did not work and he resumed amineptine at lower doses under medical supervision. But soon he felt the need and took 2 tablets every 2-3 hours. At the time of admission he was taking thirty tablets a day. Alongwith amineptine he was taking 12 mg oral bromazepam which was later increased to 45-60 mg per day in divided doses. At the time of admission mild leucocytosis and increased levels of gammaGT(154 IU/L) were recorded. Within48 hours of admission he developed an acute psychotic episode characterized by aggression and bizzare visual and auditory hallucinations. Ten days later he was discharged on request with marked improvement in his psychotic features but a strong persistent urge for amineptine.

Discussion

Clinical trials on amineptine, open and against a standard drug have demonstrated its anti-depressant activity with stimulant tendencies[1,2]. Improvement of mood is generally observed within the first week of starting treatment. The results of a double blind study[4] indicated that arnineptine acted more rapidly than amitriptyline upon depressed mood, psychomotor retardation and psychic anxiety. Its mean effective dose was two tablets (200 mg per day)[4] and increase in dose did not influence the quality of response. No case of dependence or tolerance has been reported in literature except from Pakistan[3]. Of the two cases reported by Ahmed et al. [3] one was excluded from clinical trial and treated with other anti-depressant. He improved but follow-up was not possible. In therapeutic doses a significant increase in ALT ($P<0.05$) was also observed in this study[3]. A significant increase in alkaline phosphatase was observed from the Calcutta Centre of the multi-centre study from India[5]. Inspite of massive intake over a prolonged period our cases did not show the anticipated alteration in liver bio chemistry. This confirms earlier observation that such changes may not be of clinical significance. Of interest is the motive behind the excessive use of amineptine. In case 1 feeling of increased energy and joy motivated the increased intake. These feelings would come on within 10-15 minutes of intake and last for two hours initially but later this period got reduced to half an hour. While in case 2 the main reason was to enable him to increase work output and alertness. The duration of action was similar in both the cases. In our case inspite of rigorous efforts both the patients failed to overcome the intense desire to abuse amineptine.

References

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