Treatment of tardive akathisia with clonidine: a case report

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Akathisia is characterized by subjective discomfort and motor restlessness. The motor hyperactivity can express itself by frequent changes of posture, constant limb shaking or restless pacing. If symptoms of akathisia are severe, treatment becomes extremely complicated and patients may even become suicidal as seen in the case described here.

In the literature, different forms of akathisia are distinguished (Barnes and Braude, 1985): the acute form of neuroleptic-induced akathisia (recent onset, related to an increase in antipsychotic drug dose), pseudoakathisia (motor signs but no subjective symptoms), and chronic or tardive akathisia. The acute form of akathisia is well known and described (Zubenko et al., 1984a,b). In a retrospective analysis of clinical features and therapeutic trials for tardive akathisia, Burke et al. (1989) showed that almost all of the 52 cases developed this chronic form after an average of 4.5 yr following neuroleptic drug initiation, 34% even within 1 yr. Twenty-six of the patients who were able to stop taking dopamine antagonists still had symptoms of akathisia persisting for 0.3–7 yr (mean = 2.7 yr).

As well as benzodiazepines, therapeutic regimes against acute akathisia induced by neuroleptic drugs include anticholinergics (Friss et al., 1983), amantadine (DiMascio et al., 1976) and propanolol (Lipinski et al., 1984). Efficacy of clonidine in acute akathisia was first shown in 1984 with six patients in an open on-off drug trial (Zubenko et al., 1984a) and again in 1987 with six patients under single blind conditions (Adler et al., 1987).

For chronic hyperkinetic syndromes, positive reports on the use of clonidine exist for tardive dyskinesia (Nishikawa et al., 1984). Less has been reported on clonidine for the treatment of tardive akathisia. Nishikawa et al. (1990) reported on two cases with successful clonidine treatment. Here we report an additional case of tardive akathisia responding to clonidine treatment using an on-off-on regime.

A.S. is a 57-yr-old female with a history of paranoid schizophrenia, episodic with interepisode residual symptoms (DSM-IV, 295.30) since 1984. A.S. has been hospitalized five times. Prominent symptoms were paranoia and, with increasing duration of her illness, anergia. During her first admission in 1984, she was treated with 20 mg/d haloperidol and developed marked symptoms of acute akathisia. This side-effect was successfully treated with diazepam, haloperidol was continued for more than 1 yr. During the next episode in 1993 she received 200 mg/d zotepine, which was phased out by the patient 2 yr later due to continuing akathetil symptoms. No treatment of akathisia was performed at this point. At her third hospitalization in June 1995 – with identical symptoms of akathisia – she was put on risperidone (8 mg/d). With akathisia persisting despite the use of biperiden for several weeks, she was switched to clozapine (up to 400 mg/d), leading to an amelioration both of the psychotic symptoms and the akathisia. After discontinuing clozapine in March 1996 A.S. again developed a severe paranoid syndrome with psychomotor hyperexcitability. As treatment with haloperidol alone was not efficacious, she was switched again to clozapine (300 mg/d) and later released in good clinical condition.

After discontinuation of haloperidol in March 1997 and while still on clozapine (300 mg/d), A.S. experienced a relapse in May 1997. Besides paranoia and depressed mood, prominent symptoms were difficulties with concentration and memory as well as severe akathisia. The akathetil symptoms, in particular, led to suicidal idealization.

After admission in June 1997 we increased clozapine to 450 mg/d, which successfully abolished the psychotic symptoms. Mood symptoms were treated with valproate (2100 mg/d). At this point we started to add clonidine for the persisting akathisia. The daily dosage was 75 µg for the first 6 wk. The severity of akathisia was assessed three times per week using the Barnes Akathisia Scale (Barnes, 1989). Within 2 ½ weeks the global score on the Barnes Akathisia Scale went down to zero, and the patient experienced relief from motor restlessness, expressed as constantly stamping her feet and wringing her hands.

When clonidine was discontinued akathisia reappeared after 4 d. After re-establishing clonidine, the effective dosage had to be increased to 225 µg/d. Almost 3 wk later A.S. regained her former clinical improvement without symptoms of akathisia. Even with 225 µg/d, no obvious influence on the blood pressure was noticeable.
A severe side-effect. Clonidine seems to be an efficacious letter should increase the awareness of tardive akathisia as decreasing central noradrenergic neurotransmission. This with clonidine, which acts as an evidence that tardive akathisia can be successfully treated except for clonidine, our case report gives more reliable clozapine.

causative in overcoming the potential protective effect of psychosis and discontinuation of haloperidol (withdrawal 1997. Emotional stress related to the exacerbation of her 152 whether haloperidol or other typical neuroleptics (Kurz et al., 1995), in other studies of comparable incidence (Cohen et al., 1991). For valproate, akathetic symptoms have also been observed (Gattera et al., 1994). Whereas the original improvement of akathisia can potentially also be attributed to the increase of clozapine from 300 to 450 mg, it would not explain the worsening after discontinuation of clonidine and the following amelioration of symptoms after re-instituting clonidine.

Female gender and age are considered as potential risk factors in developing neuroleptic-induced akathisia (Sandyk and Kay, 1990). With no other apparent organic cause it appears that the patient suffered from tardive akathisia, originally induced by former neuroleptic treatment and successfully controlled by clozapine until May 1997. Emotional stress related to the exacerbation of her psychosis and discontinuation of haloperidol (withdrawal akathisia; Poyurovsky et al., 1996) may have been causative in overcoming the potential protective effect of clozapine.

By using an on–off–on regime with stable medication, except for clonidine, our case report gives more reliable evidence that tardive akathisia can be successfully treated with clonidine, which acts as an α2-adrenergic agonist, decreasing central noradrenergic neurotransmission. This letter should increase the awareness of tardive akathisia as a severe side-effect. Clonidine seems to be an efficacious medication with only minor side-effects except for a possible influence on blood pressure, which was not observed in this patient. Clearly, controlled studies on the efficacy of clonidine in the treatment of tardive akathisia are still needed.

References


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Benedikt Amann, Andreas Erfurth, Heinz Grunze
Department of Psychiatry
Ludwig-Maximilians-University
Munich, Germany