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SHORT COMMUNICATION

TARDIVE DYSKINESIA TREATED WITH CLONIDINE

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INTRODUCTION

Tardive dyskinesia is a persistent and probably irreversible neurologic complication associated with long-term neuroleptic treatment. Dopaminergic supersensitivity in the brain has been postulated as a strong hypothesis on pathophysiology of tardive dyskinesia (Gerlach et al., 1974). However, dopaminergic overactivity cannot be the sole mechanism because various drugs affecting the other systems except DA neurons influenced tardive dyskinesia (Kobayashi, 1977; Jeste and Wyatt, 1979). Viukari and Linnoila (1977) reported that fusaric acid, a dopamine β-hydroxylase inhibitor relieved oro-facial dyskinesia, tremor and rigidity by reducing brain noradrenaline level. Moreover recent animal studies indicated the occurrence of α-noradrenergic receptor supersensitivity after long-term administration of haloperidol (Dunstan and Jackson, 1977; Muller and Seeman, 1977). If noradrenergic receptor supersensitivity might be involved in pathophysiology of the syndrome, clonidine, a hypotensive drug, central α-noradrenergic agonist might be anticipated to be effective by reducing noradrenaline turnover via presynaptic α-receptor stimulation or desensitization of the postsynaptic receptor (Andén et al., 1970; Svensson et al., 1975).

TABLE 1

Cases of tardive dyskinesia treated with clonidine

Case	Age	Sex	Diagnosis	Previous Treatment	Location of T.D.	Duration of T.D.	Clinical Judgement
1	57	F	hallucinatory paranoid state	yes	O	13 months	###
2	55	M	schizophrenia	yes	O, T	3 years	###
3	50	M	schizophrenia	yes	O, L	8 years	+
4	68	F	schizophrenia	yes	O	4 years	+
5	58	M	atypical psychosis	no	O	unknown	−
6	29	M	schizophrenia	no	O	1 year	+
7	40	M	schizophrenia	no	O	6 months	##
8	72	F	senile dementia	no	O	unknown	−

Abbreviations: F=female; M=male; T.D.=tardive dyskinesia; O=oral; L=limb; T=truncal Therapeutic effect was classified to four stages: remarkably improved (###); moderately improved (##); slightly improved (+); unchanged (−). No case was worsened.

As shown in Table 1, four severe cases of tardive dyskinesia (Case 1 - 4) who had not cured inspite of the previous treatments with various drugs such as thioridazine, oxypertine or amantadine for several years and four mild cases (Case 5-8) whose dyskinesia appeared within recent several months were treated with clonidine. Clonidine at daily doses of 0.15 - 0.45 mg clearly improved the symptom in several days or a month both in severe cases with daily doses of 25-150 mg of thioridazine and in mild cases with relatively high doses of neuroleptics, including two cases (Case 1, 7) whose symptoms were abolished completely without increasing finger-tapping as a provocative procedure. The trial was continued for longer than six months and in three cases (Case 4, 5, 8) the symptom tended to recur one or two months after the drug administration. No adverse effect including aggravation of psychotic symptoms was observed except transient hypotension, which disappeared in several days. Therapeutic effect of clonidine tended to be reduced by combination of high dose of haloperidol. Treatment of tardive dyskinesia with clonidine was efficacious in six of eight patients including the two (Case 1, 2) remarkably responded.

The present result showed that clonidine at the same dose as used for treatment of hypertension also had therapeutic effect on tardive dyskinesia. The blood pressure fell in almost all cases for several days after treatment but it was reversed to normal level thereafter though therapeutic effect on tardive dyskinesia was lasting for more than six months. Andén et al. (1970) reported that clonidine acted presynaptically on noradrenergic neurons within the dose range of 25-100 μg/kg and postsynaptically at the dose of more than 100 μg/kg in rats. Considering the finding, the therapeutic effect of clonidine might be initially due to reducing noradrenaline turnover via presynaptic α-receptor stimulation and subsequently due to desensitization of postsynaptic noradrenergic receptor by chronic clonidine administration. These results would contribute to the practical treatment and further understanding of the pathophysiology of tardive dyskinesia.

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