CARDIAC ARRHYTHMIA AND TRICYCLIC ANTIDEPRESSANT THERAPY

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Summary

A case has been described who developed superaventricular tachycardia, hypotension and atropine like effects on prolonged modest therapeutic dosage of tricyclic antidepressant drug amitriptyline. These side effects abated on cessation of the drug and recurred on restarting of amitriptyline, cardiac dysrhythmia was successfully treated by propranolol. The literature has been reviewed and a possibility of undue sensitivity of the patient systems to the modest therapeutic dosage of amitriptyline has been suggested.

Introduction

Cardiac arrhythmias are a common problem, when suicide attempt is made with tricyclic antidepressants but it is uncommon to observe cardiac arrhythmias, when these drugs are used in therapeutic standard dose range.

The potential hazards of tricyclic antidepressants have been recognised for the past 10 years (Kristiansen, 1961). There are reports of supraventricular tachycardia (Alexander and Nino, 1969, Ramanathan and Davidson, 1974) atrial fibrillation (Rosen, 1960), bundle branch block (Alexander and Nino, 1969, Ramanathan and Davidson 1974 and ventricular tachycardia (Scollins et al. 1972) to suggest that arrhythmias can be caused by tricyclic antidepressants. There are reports about interaction between thyroxin and imipramine (Ramanathan and Davidson, 1975) and guanethidine (Williams, 1971). Thyroxin is known to sensitize tissues to the effects of catecholamines (Harrison, 1964) which may be increased during treatment with psychotropic drugs (Carlsson et al, 1966).

A case is reported here who developed supraventricular tachycardia and hypotension with tremors during treatment with amitriptyline for depressive state, both the conditions abated on stopping the drug, recurred on restart of the antidepressant and again the symptoms resolved on stopping the drug and subsequently he had no evidence of cardiac disease.

Case Report

A male aged 35 was having antidepressant drug amitriptyline 25 mg three times a day for the past one year under psychiatrist supervision. He was seen at this Centre on 22-1-1975 with palpitation, sweating, tremores and agitation for the past one month. On examination he was agitated, exhibitea tremors of the hands, sweating, ataxia and had dizziness. Pulse was 150/minute with regular rhythm, BP 95/65 mmHg. Cardiovascular system, central nervous system and systemic examination revealed no abnormality. ECG showed supraventricular tachycardia (150/minute rate). The drug was discontinued.

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5% dextrose in normal saline 1000cc infusion raised his BP to 110/80 mmHg. He was given orally propranolol 50 mg three times a day. His pulse rate came down to 75 per minute. Two weeks later he consulted his psychiatrist for change of the drug. He was re-prescribed triptyline 25 mg t.d.s. by psychiatrist. When seen two weeks later he continued to complain palpitation and ECG showed supraventricular tachycardia (rate 150/m.). The drug was stopped and he was put on propanolol 40 mg t.d.s. to which he responded well, tachycardia and other symptoms resolved. After one week propranolol was reduced to twice a day. When seen on 25-7-1975, he was doing well on 40 mg propranolol twice a day and his pulse was 80 per minute and was free from above symptoms.

Discussion

The case was having modest therapeutic dose of amitriptyline for his depressive illness for the past one year and showed hypotension, supraventricular tachycardia with tremors, dizziness and ataxia. These symptoms disappeared on discontinuation of the drug and reappeared on restarting the amitriptyline which is suggestive that cardiovascular abnormal findings were due to the effect of the drug. There is a possibility that due to associated anxiety state catecholamines are released in this patient thus sensitizing his cardiovasular system to amitriptyline in the modest therapeutic range dose. Untoward side effects in this case on smallest dose is suggestive that severity of side effect is related to the tolerance of the individual and therefore the severity should be assessed on the clinical picutre rather than on the dose.

The most frequently reported side effects are due to the anticholinerigc properties of tricyclic depressants, occasionally these drugs precipitate excitement, sweating, dizziness, tremores and ataxia as observed in the present case (Mindham and Shepherd 1973). ECG changes resembling those produced by Quinidine are also seen. Recently cases of sudden death in patients with heart disease receiveing amitriptyline has been reported (Coull et al. 1970).

Recent Boston Collaborative drug surveillance survey programm (1972) found no higher incidence of arrhythmias in patients taking these drugs than in the rest of the hopitals population. Recently Goel and Shanks (1974) have reported cardiovascular, neurological and atropinic side effects among 60 children on these drugs (amitriptyline and imipramine) for enuresis and depression. All children were suffering from tricyclic depressants poisoning. One child of 2 years and 4 months died of posioning. They found that cardiac arrhythmias induced in children by these drugs are prominent and dangerous: Sinus tachycardia was observed in 36, sinus arrhythmia in 4, ventricular premature systoles in 3, conduction distrubance in 2, hypotension in 3 and cardiorespiratory arrest in 3 (Goel and Shanks, 1970). Two patients with severe imipramine poisoning showed conduction distrubrance: complete heart block, complete RBBB and required pacemaker. Three children with severe posioning, who took 15 mg/Kg. imipramine and 30 mg/Kg amitriptyline, required intermitent positive pressure ventilator and lignocaine 0.5 to 1 mg/minute, intravenously to control ventricular premature systoles. Two of them had ventricular tachycardia which was controlled by intravenous procainamide 700 mg and progranolol 2 mg respectively with noticeable improvement. Most of the patients with mild and moderate poison-

ing recovered spontaneously within 24 hours without sequelae as most of the drug is metabolized in 24 hours. Present case showed significant improvement in his cardiovascular status within 24 hours.

If a case is able to survive the critical first 24 hours, recovery is likely because it is during this period that most of the drug is metabolized. As there is no antidote, the management of poisoning with tricyclic is mainly symptomatic. Hong, Mauer et al. (1974) has reported a case in whom amitriptyline overdosage had resulted in transient prolongation of PR-interval, complet RBBB and possibly trifascicular block. They stressed need of availability of temporary pacing and constant ECG monitoring. The patient became comatose 6 hours after ingesting 1.5 to 2.0 Gm amitriptyline.

According to these authors prolong PR interval in their case was due to impaired conduction in the left anterior fascicle, associated with RBBB and LPH. The ECG on admission was of trifasicular block. The likelihood of this conduction abnormality to complete heart block with slow idoventricular escape rhythm has been emphasized by Rosenbaum et al. (1969).

ECG on admission showed sinus rhythm at a rate of 99 per minute, PR-interval of 0.22 sec. QRS of 0.14 sec. with secondary ST-T wave changes, RSR pattern in VI and deep S waves in V6, diagnostic of RBBB. This was associated with LPH (Left posterior hemiblock). The ECG abnormalities were reverted to normal over the next two days. Laboratory data were all within normal limits.

The mechanism of action of the tricyclic antidepressant drugs on the C.N.S. is not well understood but it is known that "catecholamines" must be present for such an effect. Cardiovascular effects on pharmacological doses in animals include anticholinergic effects with an increase in heart rate and blood pressure (Cairncross, and Gershon, 1962.).

Higher doses may cause myocardial depression with hypotension. The mechanism of action of higher doses of the drug on the cardiovascular system may be due to an ability to block the uptake of catecholamine by the heart tissues and thus exposing the catecholamines to enzymatic degradation. There is also an evidence that peripheral nerve receptor tissues are made more sensitive to catecholamines by these drugs (Axelrod et al. 1961). Chronic administration of tricyclic antidepressants has been associated with orthorstatic hypotension, tremor, nausea, vomiting, tachycardia, dry mouth, blurred vision and urinary retention (Sulser et al, 1964).

Acute intoxication is associated with central effects: agitation, restlessness, hallucination, seizure, coma, respiratory depression (Steel et al. 1967). Cardiovascular effects of acute toxication: hypertension, hypotension, tachycardia, bradycardia, congestive heart failure and myocardial infarction, ventricular extrasystole and ventricular tachycardia (Williams and Sherter, 1971).

ECG abnormalities include: all degree of conduction defects: ST depression nonspecific T-wave changes, widened QRS interval and irregular tachycardia (Freeman et al, 1969).

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