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Ventricular Arrhythmias Associated with Use of Thioridazine Hydrochloride in Alcohol Withdrawal

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Thioridazine hydrochloride (Melleril) is a widely used phenothiazine with a low incidence of extrapyramidal side effects (Kelly *et al.*, 1963). It is known to cause E.C.G. changes, which are sometimes reversed by potassium supplements (Kelly *et al.*, 1963; Alexander *et al.*, 1967). Deaths from ventricular tachycardia and fibrillation have been reported after large doses of thioridazine (Kelly, *et al.*, 1963; Alexander, *et al.*, 1967; Giles and Modlin, 1968). In the two cases reported ordinary doses of the drug in the context of alcohol withdrawal and hypokalaemia were associated with the development of ventricular fibrillation.

Case 4

A 41-year-old male alcoholic developed delirium tremens after alcohol withdrawal. He was given haloperidol 10 mg twice a day, procycladine hydrochloride 10 mg twice a day, and thioridazine hydrochloride in doses of up to 600 mg daily. Two days later he collapsed and was found to be in ventricular fibrillation. He was defibrillated and transferred to this hospital. On arrival he was unconscious and areflexic, with sluggish pupils. His blood pressure was 110/70 mm Hg. Investigations showed a serum K⁺ of 2.6 mEq/l., with normal urea and other electrolytes. He was acidotic (pH 7.32) with a base deficit of 10 mEq/l. He continued to have numerous ventricular ectopic beats, with runs of ventricular tachycardia and fibrillation. He was given KCl in 5% dextrose intravenously, 10 mEq/hr, with intravenous lignocaine at 1 to 4 mg/min and defibrillated as necessary. After 48 hours the rhythm stabilized. The serum K⁺ was 4.7 mEq/l. and the infusion was stopped. Unfortunately he remained unconscious, and after four days an E.E.G. showed a "flat" recording. Necropsy showed terminal bronchopneumonia, a fatty liver, and an area of necrosis in the posterior myocardium, without any evidence of coronary artery occlusion.

Case 2

A 41-year-old woman was admitted to hospital for alcohol withdrawal. She was given thioridazine 600 mg daily. Two days later she collapsed with a tachycardia and an unrecordable blood pressure. She became cyanosed and semiconscious and was transferred to this hospital. On arrival she was noted to be in ventricular

tachycardia, which reverted to sinus rhythm after a D.C. shock of 100 joules. Her serum K⁺ on arrival was 2.3 mEq/l., and she was acidotic (pH 7.26) with a base deficit of 14.5 mEq/l. During the next two hours she had 12 episodes of ventricular fibrillation, which were reversed by D.C. shock. She received 50 mEq sodium bicarbonate intravenously, followed by an infusion of lignocaine at 2 mg/min. An injection of 10 mEq KCl in dextrose was given directly into the subclavian vein, followed by 60 mEq KCl in dextrose over the next four hours. At this time her condition had improved. Blood gases were now normal, but the serum K⁺ remained low at 2.7 mEq/l. The infusion of KCl was continued at 10 mEq/hr, and she was started on effervescent potassium chloride, four tablets four times a day. Nine further episodes of ventricular fibrillation were aborted by D.C. shocks of 100-200 joules. Twenty-four hours after admission she was in sinus rhythm. Serum K⁺ was 3.4 mEq/l. The E.C.G. showed prominent U waves, but no evidence of infarction. The patient recovered, and was discharged with a normal E.C.G., and a serum K⁺ of 4.6 mEq/l.

Comment

E.C.G. changes reported in patients taking more than 200 mg of thioridazine daily include abnormal Q-T intervals, U waves, and T wave changes (Kelly, *et al.*, 1963; Wendkoss, 1964; Huston and Bell, 1966; Alexander, *et al.*, 1967). Fatal ventricular fibrillation has occurred in patients taking over 2 g of the drug daily (Giles and Modlin, 1968; Shoonmaker *et al.*, 1966). Atrophy of the myocardium, with fragmentation of the cell cytoplasm, has been noted at necropsy in these cases and may be an effect specific to phenothiazines (Kelly, *et al.*, 1963; Giles and Modlin, 1968).

The cases reported here were treated with thioridazine to ameliorate withdrawal symptoms. Both patients developed ventricular fibrillation after modest doses of the drug, and both were found subsequently to be severely depleted of potassium. Hypokalaemia is a recognized complication of alcoholism and is probably due to a poor diet. Replacement by intravenous potassium chloride improved the arrhythmia in both cases. The area of myocardial necrosis, without any coronary artery occlusion, noted at necropsy in the first case may represent a specific phenothiazine-induced lesion.

It is important to identify situations in which the use of a normally safe drug may be hazardous. Thioridazine has found a place in the treatment of alcohol withdrawal. Some of these patients may be potassium depleted, and its use in this context is potentially dangerous. Determination of the serum K⁺, an E.C.G., and possibly potassium supplements should accompany the use of the drug in alcohol withdrawal.

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