Pindolol-induced tremor

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Summary

Five patients were treated with pindolol for various indications. The patients called attention to the appearance of fine tremors in their extremities 6-72 hr after starting treatment with the drug. The tremors disappeared 24-72 hr after stopping the drug. Beta-adrenoceptor-blockers are known to suppress different types of tremor and the paradoxical appearance of tremors during pindolol treatment is attributed to its powerful partial agonist activity.

To the best of the authors' knowledge this side effect has not been previously described in the literature.

Introduction

Beta-adrenoceptor antagonists are widely used in the treatment of hypertension, angina and arrhythmias, and recently have also been used in the management of migraine (Ludvigsson, 1973); thyrotoxicosis (Howitt and Rowlands, 1966; Parsons and Jewitt, 1967); psychosis (Steiner *et al.*, 1972; Yorkston *et al.*, 1974); anxiety (Nissen, 1977); alcoholism, and opiate addiction (Carlsson and Johansson, 1971; Grosz, 1972, 1973; Block and Grosz, 1974); and different types of tremor (Owen and Marsden, 1965; Thompson, 1972, 1977; Winkler and Young, 1974). Pindolol is a β -adrenoceptor antagonist that possesses powerful partial agonist activity (Wagner, 1973; Aellig and Sammel, 1973; Louis, McNeil and Drummer, 1977; Robik, Jenning and Korner, 1977).

Five patients are described who paradoxically developed tremors in their upper extremities while receiving pindolol treatment for various indications.

Case reports

Case 1

A 69-year-old diabetic, hypertensive woman was admitted to hospital for an acute anterior myocardial

infarction. She was treated with propranolol and diuretics for her hypertension. Propranolol was replaced by pindolol 2.5 mg twice daily when signs of congestive heart failure appeared.

On the third day of pindolol treatment a fine tremor appeared in her upper extremities: 24 hr after cessation of the drug the tremor disappeared. Four months later she accidentally received pindolol 5 mg thrice daily, and the tremor reappeared. Again, 24 hr after stopping the drug the tremor disappeared.

Case 2

A 55-year-old man known for many years to have suffered from severe coronary artery disease, duodenal ulcer and rheumatoid arthritis, underwent a coronary bypass operation one year before admission to hospital. His recurrent anginal syndrome was treated with oxprenolol without effect. He was then treated with pindolol 5 mg times 4 daily and within a few days a fine tremor was noticed in both hands, which disappeared 24 hr after stopping the drug.

Case 3

A 20-year-old man, known to have suffered from systemic lupus erythematosus with renal involvement and hypertension, was treated with corticosteroids, azathioprine, diuretics and propranolol. Three days after propranolol had been replaced by pindolol 5 mg thrice daily, a fine tremor was noticed in both his hands; this disappeared 24 hr after the drug was discontinued.

Case 4

A 58-year-old woman, known to have suffered from hypertensive cardiovascular disease, angina and recurrent supraventricular tachycardia, showed signs of increased congestive heart failure after propranolol treatment. Within a few hours of replacing propranolol with pindolol 2.5 mg daily, the patient

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complained of a tremor in her hands; this disappeared one day after stopping the drug.

Case 5

A 66-year-old man was known to have suffered from hypertension and coronary artery disease. During treatment with propranolol and hydrallazine he developed signs of left heart failure and, as a result, propranolol was replaced by pindolol 2.5 mg twice daily. Twenty-four hours later a fine tremor appeared in his upper extremities; this disappeared 3 days after stopping the drug.

Discussion

All 5 patients developed tremors following pindolol administration. So far as the authors can ascertain from the literature, this side effect has not before been described. The tremors appeared from a few hours up to a few days after commencement of the drug and disappeared 24–72 hr after stopping it.

All 5 patients complained of, and were disturbed by, the tremors.

A connection between tremor and the adrenergic system was demonstrated by Marsden *et al.* (1967) who induced tremors with isoprenaline infusion; these tremors were immediately stopped by infusion of propranolol.

The actual mechanism by which propranolol acts on different types of tremor, whether it be via the tremorogenic receptors in the musculo-skeletal system, or via the CNS (Young, Growdon and Shanani, 1975) remains unclear. Some β -adrenoceptor-blocking agents including pindolol, paradoxically produce some stimulation of β -adrenoceptors. This property is called partial agonist or intrinsic sympathomimetic activity (ISA) activity.

Aellig (1977) and Morgan *et al.* (1974) have explained the paradoxical elevation of BP in some patients by the ISA of some β -blockers (Waal-Manning and Simpson, 1975). In contrast to propranolol, which is known to suppress different types of tremor, pindolol treatment has revealed the presence of tremors in patients who were initially tremor-free.

It is concluded that the paradoxical appearance of tremor during pindolol treatment is due to the powerful ISA of this drug.

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