Antidepressant blood levels in acute overdose

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Summary

Plasma antidepressant levels and clinical condition were measured sequentially for at least 24 hr in eight patients who presented with acute antidepressant overdosage. There was no evidence to suggest that a knowledge of the drug plasma levels had anything to offer in the management of a patient whose overdose included a tricyclic antidepressant.

Introduction

Tricyclic antidepressants are widely prescribed drugs and feature prominently as agents used in self poisoning. A wide range of complications in overdose have been recognized: cardiac conduction disturbances and arrhythmias; respiratory depression; convulsions; hyperpyrexia and psychosis. Death can also occur (Sedal *et al.*, 1972; Asberg *et al.*, 1971). Interest has recently been aroused in the relationship between plasma levels of antidepressants and the various expressions of their effect. Considerable individual variation in plasma levels of drug have been demonstrated for a fixed oral dose, and plasma levels show a closer correlation with pharmacological action than does oral dose. Debate at present exists as to the precise significance of the plasma drug level related to the therapeutic response, but therapeutic levels of amitriptyline are rarely encountered above 200 ng/ml (Asberg *et al.*, 1971; Braithwaite *et al.*, 1972).

Any possible relationships between the plasma antidepressant levels and the physiological measures made on patients who presented with overdoses were investigated.

Method

Eight patients who had taken tricyclic antidepressant overdoses were studied. Blood was taken on admission and at approximately 6, 12 and 24 hr after. At the same time, a rating form was completed with special reference to severity of disturbances of consciousness. Temperature, pulse rate,

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ECG abnormalities and any other relevant findings were noted. The plasma was deep frozen and subsequently analysed by gas chromatography (Gifford, Turner and Pare, 1975).

Results

The condition of four patients was critical on general clinical grounds. They required supportive measures and were deeply unconscious for about 18 hr. In four of the eight patients the fall in plasma levels followed that of returning consciousness. In two patients the correlation was poor and in two the clinical condition deteriorated as the plasma drug level fell. There was no correlation between the plasma drug level and the clinical severity of the overdose, ECG changes, variations in temperature, pulse rate change, or anticholinergic side effects on return to consciousness. Ventricular ectopic beats occurred for the first time in a patient at a drug concentration of 320 ng/ml, the level having fallen from 510 ng/ml since admission.

All patients showed a reduction of plasma drug levels within 20 hr but gastric lavage even in the first 3 hr after drug ingestion did not prevent a further rise in plasma drug level. Plasma nortriptyline levels in no case rose above 50 ng/ml.

Conclusion

In half the patients the clinical condition improved as plasma drug level fell. Otherwise there was no correlation between plasma drug levels or their change with any of the parameters measured.

There was, therefore, no evidence to suggest that knowledge of plasma drug levels or sequential levels have anything to offer in the management of a patient whose overdose included a tricyclic antidepressant.

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TABLE 1. Synopsis of significant findings

Patient no.	Age (years)	Drugs taken	Gastric lavage	Drug serum level (ng/ml)		Comment
				On presentation	Maximum	
1	40	Imipramine Alcohol Chlordiazepoxide	No	190	220	Unconscious for 15 hr
2	19	Amitriptyline	Yes	288	740	Clinically mild. Level rose as consciousness improved
3	56	Amitriptyline Chlordiazepoxide	No	510	510	Despite serum level falling required to be ventilated 20 hr after drug ingestion. Developed ventricular ectopic beats at a serum level of 320 ng/ml
4	60	Amitriptyline	Yes	300	450	Clinically mild
5	23	Amitriptyline Nitrazepam Diazepam	Yes	620	620	Clinically mild
6	23	Amitriptyline	Yes	300	410	Clinically mild
7	59	Imipramine Diazepam Alcohol	Yes	580	580	Unconscious for 36 hr. Hallucinated on recovery
8	43	Amitriptyline	Yes	110	110	Time of overdose unknown. Clinically severe.

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