SHORT REPORTS

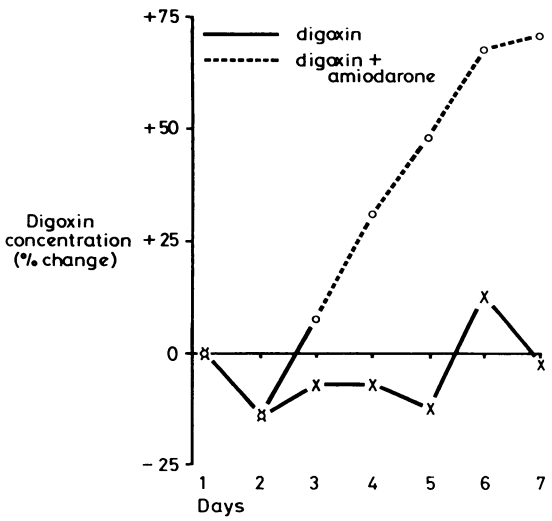
Amiodarone increases plasma digoxin concentrations

As treatment regimens become more complex the dangers of drug interaction increase. We observed that several patients receiving maintenance digoxin treatment abruptly developed clinical evidence of toxicity when amiodarone, a newly available antiarrhythmic agent, was administered in addition. We therefore studied several patients to determine the response of plasma digoxin concentrations to treatment with amiodarone.

Patients, methods, and results

Seven patients receiving maintenance digoxin treatment were given amiodarone to control refractory arrhythmias. All had paroxysmal or sustained atrial fibrillation and three had had other supraventricular arrhythmias. Maintenance doses of digoxin had been constant for at least two weeks before the study. Plasma digoxin concentrations were measured daily for seven days using a radioimmunoassay technique[1]; samples were drawn eight hours after administration of digoxin.

On days 3-7 amiodarone 200 mg was administered thrice daily; plasma digoxin concentrations increased progressively by an average of 69% (mean 1·17 to 1·98 μg/l (figure). Four patients developed symptoms compatible with digoxin toxicity.



Mean percentage change in daily plasma digoxin concentrations in seven patients treated with digoxin with amiodarone added from day 3 (o) and six controls treated with digoxin alone (x).

Two additional patients were studied in a similar manner, but maintenance amiodarone was increased from 200 to 600 mg daily rather than introduced on the third day. Plasma digoxin concentrations increased by 0·4 and 0·7 μg/l respectively over the subsequent five-day period.

Plasma digoxin concentrations were measured daily for seven days in six patients with supraventricular arrhythmias receiving maintenance digoxin alone. No trends towards increased concentrations were found. At no time were falsely positive results of digoxin assays obtained in four patients taking amiodarone alone. Amiodarone added in vitro did not affect the results of the radioimmunoassay. Four of the patients given amiodarone and all six controls were admitted to hospital from the first day of the serial observations.

Comment

Amiodarone is a powerful antiarrhythmic agent unrelated to conventional drugs and widely used in Europe and South America. Though introduced in 1967, it has only recently been licensed for use in Britain. It is most often used alone but also serves as a useful adjunct to digoxin in the treatment of supraventricular arrhythmias inadequately controlled by cardiac glycosides.[2] Thus the finding that amiodarone increases plasma digoxin concentrations and perhaps precipitates some manifestations of toxicity is of considerable practical importance. Quinidine also increases plasma digoxin concentrations.[3]

Our observation was based on manifestations of neurotoxicity and unexpectedly high plasma digoxin concentrations in several patients newly treated with amiodarone but previously managed with stable digoxin regimens. During the subsequent study, which did not include the patients who originally showed toxicity, all patients showed progressive increases in digoxin concentrations after amiodarone was added or its dosage increased. An increase in plasma concentration because of better compliance seems an unlikely explanation for every patient, especially since none of our control group showed this tendency. Results of digoxin radioimmunoassay were always negative in patients receiving amiodarone treatment alone, and we found no evidence of interference in the assay when amiodarone was added in vitro.

Amiodarone is avidly tissue bound, and concentrations of digoxin in some tissues are more than 100 times those found in plasma.[4] Amiodarone may displace tissue-bound glycoside or interfere with digoxin excretion, but the mechanism has not yet been investigated in detail. High plasma concentrations of digoxin without commensurate increases in myocardial concentrations would be expected to cause neurotoxicity rather than direct cardiac toxicity; but heart rhythm may be influenced by both mechanisms.[5]

We do not know whether the interaction we have noted is dangerous in terms of arrhythmogenic potential, but nausea and other manifestations of glycoside toxicity that occur may be interpreted incorrectly as a direct effect of amiodarone, leading to inappropriate modification to treatment. Our present practice is to halve maintenance digoxin doses when amiodarone is introduced.

[1] Smith TW, Butler VP Jr, Haber E. Determination of therapeutic and toxic serum digoxin concentrations by radioimmunoassay. *N Engl J Med* 1969;**281**:1212-6.
[2] Wheeler PJ, Puritz R, Ingram DV, Chamberlain DA. Amiodarone in the treatment of refractory supraventricular and ventricular arrhythmias. *Postgrad Med J* 1979;**55**:1-9.
[3] Ejvinsson G. Effect of quinidine on plasma concentrations of digoxin. *Br Med J* 1978;i:279-80.
[4] Coltart J, Howard M, Chamberlain D. Myocardial and skeletal muscle concentrations of digoxin in patients on long-term therapy. *Br Med J* 1972;ii:318-9.
[5] Gillis RA, Pearle DL, Levitt B. Digitalis: a neuroexcitatory drug. *Circulation* 1975;**52**:739-42.

(*Accepted 5 November 1980*)

Department of Cardiology, Royal Sussex County Hospital, Brighton BN2 5BE

J O MOYSEY, MB, BS, lately research senior house officer
N S V JAGGARAO, BSC, MRCP, research registrar
E N GRUNDY, PHD, principal biochemist
D A CHAMBERLAIN, MD, FRCP, consultant cardiologist

Home blood glucose monitoring: a sticky artefact

Monitoring blood glucose concentrations at home is now established in diabetic management[1] and is used by many diabetic children attending the Oxford Paediatric Diabetic Clinic. Some families find it particularly useful to be able to measure their child's blood glucose concentration after treatment of a nocturnal hypoglycaemic episode and thus differentiate drowsiness due to continuing hypoglycaemia from the natural desire to go back to sleep. Great care should be used in the procedure, however, since contamination with glucose may result in a false reading.

Case report

A 14-year-old diabetic boy woke his parents after a nightmare at 2 am. His blood glucose concentration was measured using an indicator stick and capillary blood from a finger. It was <2 mmol/l (36 mg/100 ml), and with a slight struggle (because he was confused) his parents encouraged him to swallow 15 ml 100% glucose-maltose solution. Despite this he became increasingly drowsy and unrousable over the next half-hour. At 3 am his