

Fatal digoxin overdose

D. P. NICHOLLS
M.B., M.R.C.P.

Department of Medicine, Hope Hospital, Salford

Summary

Overdosage with cardiac glycosides is well documented, but not usually fatal. A case is described in which cardiac arrest in asystole was associated with a serum digoxin level of 50.4 µg/l, the highest concentration yet reported after oral administration.

Introduction

In various series of cases of overdosage with cardiac glycosides, the overall mortality has been 13% (Bergy, Fergus and Bruce, 1957), 20% (Gaultier *et al.*, 1968), and 22% (Bismuth *et al.*, 1973). Another series has included measurement of serum digoxin levels (Somogyi, Kaldor and Jankovics, 1972). The highest level previously recorded after oral administration was 42.0 µg/l (Smith and Willerson, 1971).

Case report

A 54-year-old woman was admitted to the Tameside General Hospital about 90 min after taking an unknown quantity of digoxin BP 0.25 mg tablets, and a diuretic (hydrochlorothiazide 50 mg, with amiloride 5 mg). Seven months previously, she had presented with acute pulmonary oedema, which was found to be due to mitral stenosis, and treatment with digoxin 0.25 mg b.d. and the diuretic two tablets daily was commenced. In addition, she had recurrent depression for which she had received ECT and tricyclic antidepressive drugs in the past. At the time of admission, her only other medication was chloral hydrate 15 ml at night.

On admission, she was semi-conscious, pale, sweating and vomiting, with a bradycardia of 26 beats/min and an unrecordable blood pressure. Monitoring showed prolongation of the P-R interval, and an Elecath transthoracic bipolar pacing catheter was inserted into the right ventricle. Ventricular fibrillation was produced, and sinus rhythm restored by DC defibrillation; demand pacing was established at a rate of 80 beats/min but required maximum output (25 mA). Sodium bicarbonate, 200 mmol, was infused. There was some clinical improvement, and the monitor showed atrial fibrillation with a ventricular rate of 130 beats/min.

Correspondence: Dr D. P. Nicholls, Hope Hospital (University of Manchester School of Medicine), Eccles Old Road, Salford M6 8HD.

inhibiting the pacer. Deterioration in clinical state was associated with multifocal ventricular ectopic beats, and she quickly developed ventricular tachycardia and fibrillation despite lignocaine 100 mg intravenously. DC defibrillation produced asystole, and there was no response to isoprenaline 100 µg or potassium chloride 25 mmol intravenously. The heart was exposed via a left-sided thoracotomy, but there was no response to internal cardiac massage or to suturing the pacing wires directly to the myocardium. Death was presumed some 2 hr after admission.

Post-mortem examination revealed congestion of the lungs and liver and an empty stomach. The heart weighed 340 g with a left ventricular myocardial thickness of 14 mm. The mitral valve was thickened and calcified. There were a few purpuric spots on the pericardial surface of the ventricles and an area of endocardial haemorrhage in the left ventricle.

Analysis of the blood showed a salicylate concentration of 0.16 mmol/l and a digoxin concentration of 50.4 µg/l measured by radioimmunoassay. The Wellcome 'Lanoxitest B' kit was used with a modified method (Ojala, Karjalainen and Reissell, 1972).

Discussion

Serum digoxin levels in excess of 50 µg/l are transiently reached during intravenous loading (Bertler, Bergdahl and Karlsson, 1974). Self-administration of 200 mg of digoxin intravenously produced a peak level of 52.0 µg/l and the patient subsequently died (Reza *et al.*, 1974). Administration of digoxin specific antibodies may cause a sharp rise in total serum digoxin concentration (Smith *et al.*, 1976). A post-mortem level of 0.15 mg/l has been reported (Steenoft, 1973), but this was assayed by fluorometry, which is not as sensitive as radioimmunoassay (Marks, Lindup and Baylis, 1973).

The complications and management of digoxin overdosage have been described elsewhere (Leading Article, 1972); the main complications are hyperkalaemia and cardiac arrhythmias. Hyperkalaemia is an important feature of severe digoxin poisoning and the initial serum potassium levels are related to the mortality (Bismuth *et al.*, 1973; Smith and Willerson, 1971; Doherty, 1968). The hyperkalaemia is thought to be due to failure of the ATPase membrane pump

and consequent leakage of potassium from the myocardial cells (Glynn, 1964). Attempts to control the hyperkalaemia, including using haemodialysis, may be unsuccessful (Reza *et al.*, 1974; Smith and Willerson, 1971). Little attention was paid to potassium balance in the present patient owing to the rapidity of events, but this probably made little difference to the fatal outcome. Other unfavourable factors in this case include the previous maintenance therapy, which may have saturated the drug-binding sites, and the relative intolerance of diseased myocardium to digoxin.

One of the commonest cardiac arrhythmias is bradycardia with varying degrees of atrioventricular block. Atropine may be tried, but pacing is usually required. In the presence of hyperkalaemia, a pacemaker should be inserted as a prophylactic measure even if the ECG is normal (Bismuth *et al.*, 1973). However, in fatal cases there is often terminal resistance to pacing. In the present case, there was complete cardiac standstill despite direct electrical stimulation of the myocardium. This too seems to be due to failure of the myocardial cell membrane pump (Reza *et al.*, 1974).

The recent description of digoxin-specific antibodies and their use in severe digoxin poisoning may be a significant advance (Smith *et al.*, 1976); in the case they report, hyperkalaemia and pacing resistance were both reversed and the patient survived.

Acknowledgment

I would like to thank Dr M. H. Husaini for permission to report this case.

Postgraduate Medical Journal (May 1977) **53**, 281–285.

Leiomyosarcomatosis of probable uterine origin with long survival—a case report

R. A. L. YOUNG*
F.R.C.S.

Whittington Hospital, London

Summary

A case of leiomyosarcomatosis is presented. Over a period of 15 years the patient underwent seven operations to remove eleven tumours, the largest as big as a football, before dying of widespread metastases: between operations the patient was remarkably well. The disease was almost certainly of uterine origin

* Present address: Royal Free Hospital, Pond Street, London NW3 2QG.

References

- BERGY, G.G., FERGUS, E.B. & BRUCE, R.A. (1957) Acute massive digitoxin poisoning: report of a case and review of the literature. *Annals of Internal Medicine*, **46**, 964.
- BERTLER, A., BERGDAHL, B. & KARLSSON, E. (1974) Plasma-digoxin concentrations after an intravenous loading dose. *Lancet*, **ii**, 958.
- BISMUTH, C., GAULTIER, M., BONNET, M. & POLLET, J. (1973) L'hyperkalémie dans l'intoxication digitalique massive. *Biomédecine Express (Paris)*, **19**, 152.
- DOHERTY, J.E. (1968) The clinical pharmacology of digitalis glycosides: a review. *American Journal of the Medical Sciences*, **225**, 382.
- GAULTIER, M., FOURNIER, E., EFTHYMIU, M.-L., FRÉJAVILLE, J.-P., JOUANOT, P. & DENTAN, M. (1968) Intoxication digitalique aiguë (70 observations). *Bulletin et Mémoires de la Société Médicale des Hôpitaux de Paris*, **119**, 247.
- GLYNN, I.M. (1964) The action of cardiac glycosides on ion movements. *Pharmacological Reviews*, **16**, 381.
- LEADING ARTICLE (1972) Self-poisoning with digoxin. *Scottish Medical Journal*, **17**, 263.
- MARKS, V., LINDUP, W.E. & BAYLIS, E.M. (1973) Measurement of therapeutic agents in blood. *Advances in Clinical Chemistry*, **16**, 47.
- OJALA, K., KARJALAINEN, J. & REISELL, P. (1972) Radio-immunoassay of digoxin. *Lancet*, **i**, 150.
- REZA, M.J., KOVICK, R.B., SHINE, K.I. & PEARCE, M.L. (1974) Massive intravenous digoxin overdosage. *New England Journal of Medicine*, **291**, 777.
- SMITH, T.W., HABER, E., YEATMAN, L. & BUTLER, V.P. (1976) Reversal of advanced digoxin intoxication with Fab fragments of digoxin-specific antibodies. *New England Journal of Medicine*, **294**, 797.
- SMITH, T.W. & WILLERSON, J.T. (1971) Suicidal and accidental digoxin ingestion: report of five cases with serum digoxin level correlations. *Circulation*, **44**, 29.
- SOMOGYI, G., KALDOR, A. & JANKOVICS, A. (1972) Plasma concentrations of cardiac glycosides in digitalis intoxication. *European Journal of Clinical Pharmacology*, **4**, 158.
- STEENTOF, A. (1973) Fatal digitalis poisoning. *Acta pharmacologica et toxicologica*, **32**, 353.

from apparently benign fibroids, and photomicrographs are provided as supportive evidence. The various modes of presentation of abdominal leiomyosarcoma—mass, pain, obstruction, fistula, anaemia—are illustrated in the case report. The value of repeated palliative surgery in such cases is emphasized.

Case report

At the age of 53, in 1960, the patient presented at