The Ulster Medical Journal, Volume 67, No. 1, pp. 13-18, May 1998.

Drug overdoses requiring temporary cardiac pacing;

A study of six cases treated at Altnagelvin Hospital, Londonderry

P G McGlinchey, A J McNeill

Accepted 13 March 1998

SUMMARY

Drug overdoses in general are increasing and overdoses of cardiac medications are also increasing; some are associated with a high mortality. Temporary cardiac pacing has a valuable role in cases of hypotension related to dysrhythmia, or when it is necessary to provide overdrive pacing. However, despite technically successful and uncomplicated pacemaker insertion and restoration of cardiac electrical activity, patients developing bradyarrhythmia and hypotension after an overdose are in a high risk group.

INTRODUCTION

Deliberate drug overdose is a common presentation at Accident and Emergency departments throughout the country. In the year 1st April 1996 to 3rd March 1997, 807 cases of deliberate overdose were admitted to Altnagelvin Hospital; this represents almost 12% of all medical admissions at this hospital (6745 admissions, including 2190 cardiology cases), compared with 321 cases in 1980, 290 in 1981 and 444 in 1982, when they represented 14% of acute medical admissions.[1] In the vast majority of cases, after initial assessment and treatment, most are medically well. However, a number can be in danger of either acute respiratory or cardiac arrest, which may be fatal; artificial ventilation and temporary cardiac pacing respectively may be required.

METHODS

This is a retrospective review of six known cases of drug overdose requiring temporary cardiac pacing between November 1994 and February 1997. Data were collected on age, sex, past cardiac and psychiatric history, haemodynamic signs, electrocardiographic changes, therapeutic intervention and final outcome in the six patients.

CASE HISTORIES

Case 1. A 46 year old woman was admitted having taken an overdose of 1200 mg of flecainide and an unknown quantity of sotalol at an unknown time. She had a past history of paroxysmal atrial fibrillation with an exercise stress test mildly positive for ischaemia and she had been taking these drugs prophylactically for three and a half years and nine months respectively. She had no past history of psychiatric disease or of prior overdose.

On admission to the Accident and Emergency department she was drowsy but still rousable; her heart rate was 30 beats per minute and her blood pressure (BP) 60/25 mmHg. Her ECG showed a broad complex bradycardia. She was treated initially with 3mg of intravenous atropine given as five boluses of 600 mcg. Although her heart rate rose to 53 beats per minute, her BP became unrecordable and she was transferred to the cardiology unit for emergency temporary cardiac pacing. During transit, she developed electro-mechanical dissociation. She was intubated and treated with 3 mg of intravenous adrenaline given as 1 mg boluses, along with cardiopulmonary resuscitation and inotropic support with intravenous dobutamine. A temporary pacing wire was inserted via the right supraclavicular approach; the wire was placed in a satisfactory position but there was failure to respond and the patient died.

Cardiology Unit, Altnagelvin Hospital Health and Social Services Trust, Londonderry.

P G McGlinchey, MB, BCh, BAO, Senior House Officer.

A J McNeill, MD, FRCP, FESC, Consultant Cardiologist.

Correspondence to Dr McNeill.

Case 2. A 33 year old woman presented at Accident and Emergency having taken her father's diltiazem, atenolol, isosorbide mononitrate and nifedipine. The of tablets and the time when taken were not known. She had a past psychiatric history of anorexia and severe depression requiring formal psychiatric admissions. She had no history of deliberate self-harm but has since been re-admitted with a second overdose.

She was very agitated on admission, heart rate was 35 beats per minute, systolic blood pressure 60 mmHg and ECG showed a nodal bradycardia. She was treated with an intravenous infusion of *Gelofusine*, intravenous atropine 600 mcg given three times, 10 mls of 10% calcium gluconate intravenously, intravenous glucagon 3 mg in 20 mls of 5% dextrose over five minutes and an intravenous infusion of dobutamine. As there was little improvement in her haemodynamic status a cardiac pacing wire was inserted. Blood pressure after pacemaker insertion increased to 85/33 mmHg.

The dobutamine infusion rate was increased and the blood pressure further improved to 90/50 mmHg that evening, and was 105/60 mmHg the next morning. She was later seen by the psychiatry team who felt the diagnosis was of a borderline personality disorder. The remainder of her stay was uneventful and she was discharged.

Case 3. A 17 year old boy was transferred from another hospital for temporary pacemaker insertion. He had presented there at 12.30 am having taken an overdose of digoxin 15 mg, mefenamic acid 2000 mg and *Tylex* (two tablets) at 10 pm the previous night. He had a history of depression and had three previous admissions following overdose in the past. Cardiac monitoring showed him to be having episodes of asystole lasting up to six seconds, and episodes of ventricular bigeminal rhythm. A digoxin level taken at 5 am had shown a level of 10.77 mcg per litre (therapeutic range 0.8 to 2.0). His initial heart rate was 89 beats per minute and blood pressure 155/88 mmHg, both of which had been maintained despite his arrythmias. He was transferred to Altnagelvin hospital for temporary cardiac pacing.

On arrival he was awake and alert, heart rate was 74 beats per minute and blood pressure 137/82 mmHg. ECG showed sinus rhythm with ST changes attributable to digoxin ("reverse tick"). He was treated initially with 12 vials of *Digibind* and later with a further 4 vials. In view of his documented periods of asystole, a temporary pacing wire was inserted via the right subclavian vein without complication, and capture was achieved. Temporary pacing was only required for a short time after return to the Coronary Care Unit as the patient remained in sinus rhythm without pauses after further administration of *Digibind.*

The serum digoxin level gradually decreased to acceptable levels. No further periods of asystole were noted and he remained haemodynamically stable and the wire was removed. He was seen by the psychiatry team who felt there was no evidence of mental illness and that the overdose had been an impetuous gesture.

Case 4. A 20 year old lady presented to the Accident and Emergency department having taken an overdose of 20 tablets of quinine sulphate 300 mg (total dose 6000 mg) two hours prior to her arrival. She had no relevant past medical history. The medication belonged to a relative.

On arrival she was drowsy but rousable; she complained of having hearing loss but initially had no visual disturbance. Although her heart rate was 108 beats per minute and blood pressure 115/60 mmHg, the ECG showed right axis deviation and first degree heart block. Gastric lavage was performed and she was also given activated charcoal. Blood sent for analysis later showed a quinine level of 20.6 mg/l (toxic levels >10.0 mg/l) and a potassium concentration of 2.6 mmol/l. Intravenous fluids containing potassium supplementation were commenced. She complained later of having total loss of vision and her pupils were found to be dilated and non-reactive.

Soon after admission she developed ventricular tachycardia, but her blood pressure was well maintained and she was treated with a bolus of amiodarone 150 mg intravenously, followed by an infusion of amiodarone (900 mg over 24 hours). Forty minutes after admission she developed a tonic-clonic seizure lasting 5 minutes which resolved with the administration of 5 mg of intravenous diazepam. Post-seizure monitoring showed her to be in persistent ventricular tachycardia with a good blood pressure (120/50 mmHg). She was treated with DC cardioversion, requiring shocks of 100J and then 200J before sinus rhythm returned. It was felt that temporary pacing was required as a prophylactic measure, given the combination of first degree atrio-

ventricular dissociation and ventricular tachycardia. Temporary pacemaker insertion was successfully performed via the right femoral vein as the subclavian and internal jugular veins could not be entered due to the patient's agitation. Overdrive pacing was not required.

The remainder of her stay was unremarkable from a cardiac viewpoint. Her heart rate and blood pressure were well maintained and there were no further episodes of ventricular tachycardia. Her hearing returned to normal quite quickly and her vision made similar, but slower, progress. She was seen by the psychiatry team who did not find her to be mentally unwell, and she was discharged.

Case 5. A 32 year old man was admitted having taken an overdose of 1200 mg of diltiazem, 900 mg of isosorbide mononitrate and possibly bisoprolol while under the influence of alcohol about three hours previously. He had a past history of ischaemic heart disease with an inferolateral myocardial infarction and subsequent episodes of angina requiring hospital admission. He had a prior diagnosis of depression, which was felt to be reactive, and also of phobic anxiety, but he had not taken an overdose before. The medications taken were for his own use.

He was drowsy on admission but awake; his pulse rate was 48 beats per minute, blood pressure 40/10 mmHg and ECG showed a nodal bradycardia. He was treated with gastric lavage, charcoal, intravenous atropine 1200 mcg in two equal doses and 10 mls of 10% calcium gluconate initially. Blood alcohol level was 198 mg%. The heart rate improved to 61 beats per minute and the blood pressure rose to 60/40mmHg. He was commenced on intravenous infusions of dobutamine and dopamine to provide inotropic support.

The following morning his blood pressure had risen to 78/44 mmHg but he remained bradycardic at 50 beats per minute. ECG continued to demonstrate a nodal bradycardia. For this reason (nodal bradycardia with hypotension) a temporary cardiac pacing wire was successfully inserted via the left supraclavicular approach.

Blood pressure rose to 105/70 mmHg following this procedure and he was gradually weaned off both dopamine and dobutamine. Haemodynamic stability was restored and the pacing wire was removed. He was seen by the psychiatrists who offered him admission to the local psychiatric hospital but this was declined and he was discharged.

Case 6. A 14 year old boy presented at the Accident and Emergency department via ambulance having taken an overdose estimated at 2800 mg of atenolol and 5400 mg of diltiazem around ten hours prior to admission. The drugs taken were not for his personal use and his past medical history was totally unremarkable.

On admission he was drowsy but still able to communicate coherently. His heart rate was 51 beats per minute, blood pressure 60/31 mmHg and ECG showed a nodal bradycardia. Twenty minutes later his heart rate dropped to 36 beats per minute with an unrecordable blood pressure. He was treated with intravenous atropine 3 mg given in five boluses of 600 mcg, 10 mls of 10% calcium gluconate, 1 mg of intravenous glucagon, intravenous *Gelofusine* and was commenced on an intravenous infusion of dobutamine; it was decided that temporary cardiac pacing was necessary. Before transfer to the cardiology unit he developed asystole which was treated with cardiopulmonary resuscitation and intravenous boluses of adrenaline; he was successfully resuscitated and moved immediately to the Cardiology unit where a temporary cardiac pacing wire was inserted via the left supraclavicular approach without difficulty. He subsequently developed electromechanical dissociation with a satisfactory pacing rhythm on the monitor but he had no palpable cardiac output and no ventricular systole was seen on X-ray screening of the mediastinum. He had been intubated and was commenced on cardiopulmonary resuscitation combined with intensive inotropic support with high dose adrenaline, noradrenaline, dobutamine and *Gelofusine*. He also received further doses of calcium gluconate and glucagon. Although he had a strong output with CPR, no spontaneous cardiac output was detected despite clear electrical activity on monitor. After a period of resuscitation which lasted three hours in total with no detectable recovery, this was discontinued and he was pronounced dead.

DISCUSSION

Although these data are retrospective and uncontrolled, we feel that they are useful indicators of the type of rhythm disturbance that

TABLE

Summary of information in the six cases presented

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	46 years	33 years	20 years	17 years	32 years	14 years
Sex	Female	Female	Female	Male	Male	Male
Cardiac History	Paroxysmal atrial fibrillation; mildly positive EST	None	None	None	Myocardial infarcation; angina	None
Psychiatric History	None	Anorexia, Depression, Personality disorder	None	Depression	Depression; Phobic anxiety	None
Prior Overdose	None	No, but one since	No	Three known	None	None
Drugs taken and dosage	Flecainide 1200 mg; Sotalol (unknown dose)	Diltiazem, Atenolol, Isosorbide mononitrate Nifedipine (doses unknown)	Quinine sulphate 600 mg	Digoxin 15 mg; Mefenamic acid 2 g; Tylex 2tabs	Diltiazem 1200 mg; Isosorbide momonitrate 900 mg; ?Bisoprolol	Atenolol 2800 mg; Diltiazem 5400 mg
Time until presentation after taking overdose	Unknown	Unknown	2 hours	2 hours, 30 mins	3 hours	10 hours
Heart rate on admission	30 bpm	35 bpm	108 bpm	89 bpm	48 bpm	51 bpm
Blood pressure on admission	60/25 mmHg	60 mmHg systolic	115/60 mmHg	155/88 mmHg	40/10 mmHg	60/31 mmHg
ECG findings	Broad complex bradycardia	Nodal bradycardia	Right axis deviation; first degree heart block, ventricular tachycardia (later)	Episodes of asystole; ventricular bigeminy	Nodal bradycardia	Nodal bradycardia
Indication for pacing	Bradycardia with hypotension	Bradycardia with hypotension	Persistent ventricular tachycardia	Episodes of asystole up to 6 secs	Bradycardia with hypotension	Bradycardia with hypotension
Blood pressure after pacing		85/33 mmHg	132/71 mmHg	97/55 mmHg	105/70 mmHg	
Outcome	Dead	Alive	Alive	Alive	Alive	Dead

may occur after overdose of cardiotoxic medications. It is impossible to prove whether pacing influences the outcome in these patients, but it would be unethical and clinically unacceptable to withhold temporary pacemaker insertion in a patient with documented bradydysrhythmia and hypotension; given the negative chonotropic effects of all the drugs ingested, temporary pacemaker insertion is a rational therapy to adopt.

Although deliberate drug overdose is a common reason for acute medical admission to hospital, few such cases require temporary cardiac pacing. However, the mortality in this group of patients is an indicator of the worrying prognosis in patients who require temporary cardiac pacing as a consequence of drug-induced arrhythmias. Beta-blockers and calcium channel blockers were the drugs most commonly implicated. Calcium channel blockers are increasingly prescribed for hypertension, angina and arrhythmias and with their rise in popularity there has been an increase in the incidence of overdose of these drugs.[2, 3]

Three of the six cases described involved overdose of calcium channel blockers; all presented with nodal bradycardia and hypotension which are predictable from their pharmacological action on the myocardium, vascular smooth muscle and cardiac conducting system.[4] Other clearly documented side effects include sinus bradycardia, accelerated atrioventricular node conduction, second and third degree heart block.[5]

The ideal emergency treatment of calcium channel overdose has yet to be defined, but includes calcium, glucagon, atropine, isoproterenol, dopamine, dobutamine, adrenaline and noradrenaline.[2] The administration of calcium is not always effective in treating overdoses of a calcium channel blocker, but clinical improvement has been demonstrated in most instances.[3]

The use of cardiac pacing in calcium channel blocker overdose has been mentioned in a number of sources with an overall positive response but also acknowledgment that there may be a failure to capture successfully or with no haemodynamic improvement, as in case 6.[2, 3, 5]

Beta adrenergic blocking agents are used in angina, hypertension and as anti-arrhythmic agents. The usual clinical manifestations of beta-blocker overdose include bradycardia, hypotension, low cardiac output, cardiac failure, cardiogenic shock, bronchospasm, respiratory failure, seizures and prolonged intraventricular conduction.[6]

The haemodynamic compromise induced by beta-blocker overdose usually responds to sympathomimetics, parasympatholytics, glucagon, phosphodiesterase inhibitors and cardiac pacing. Glucagon in particular has been proposed as the drug of choice due to its effect in increasing levels of intracellular cyclic adenine monophosphate (cAMP) independently of adrenergic receptors. Cardiac pacing has been documented in addition to glucagon as the treatment of first choice for the management of beta-blocker overdose.[6]

Flecainide is a class 1C anti-arrhythmic drug indicated for the treatment of ventricular and supraventricular dysrhythmias including Wolff-Parkinson-White syndrome. In general, overdose with this class of drug is associated with a high mortality.[7] It is felt that there is a correlation between toxic levels in the blood and ECG changes, in particular broadening of the QRS complex. Other ECG changes reported include prolongation of the PR interval, right bundle branch block and giant inverted T waves. Flecainide has a negative inotropic effect which has been suggested as the cause of the profound hypotension seen in many cases of overdose. Survival after overdose is associated with persistent ECG changes lasting more than 15 days. The hypotension has been found to respond to intravenous dobutamine, dopamine and isoprenaline.[7]

Quinine is used for the treatment of nocturnal leg cramps, malaria and myotonia. As it is an optical isomer of quinidine, a class 1A anti-arrhythmic drug, quinine and quinidine have a number of cardiotoxic effects including sinus tachycardia, sinus bradycardia, widening of the QRS complex, prolongation of the PR and QT intervals, atrioventricular blocks, broad complex tachycardias, torsades de pointes and idioventricular rhythms. Other effects include tinnitus, deafness and visual disturbance.[8]

Standard poisoning treatment and supportive care are the mainstay of therapy in quinine poisoning. Therapeutic inotropic support and cardiac pacing may be required.[8]

Digoxin is used in the treatment of atrial fibrillation, paroxysmal supraventricular

tachycardia, atrial flutter, and in cardiac failure. Because of its effects on the myocardium, sinoatrial and atrioventricular nodes via the vagus nerve, digoxin in overdose will induce arrhythmias including ventricular ectopic beats, ventricular tachydysrhythmias, paroxysmal supraventiicular tachycardia and heart block. Death from digoxin intoxication usually results from ventricular fibrillation, asystole, pump failure or from mesenteric infarction.[9]

Digoxin overdose is treated by use of digoxin-specific Fab antibody fragments as antidote.[10] Indications for pacing include severe bradycardia (mostly secondary to atrioventricular block or to sinoatrial block) and hyperkalaemia > 5 mmol/L.[9] There had been a suggestion that during digoxin poisoning, the fibrillary threshold is lowered and thus cardiac pacing may lead to overdrive inhibition of spontaneous rhythms. Although the failure rate with use of the pacemaker was higher than with use of the Fab antibody fragments, the difference was not significant.[9]

ACKNOWLEDGEMENTS

We wish to thank the staff of the Medical Records Department and the Medical Library in Altnagelvin Hospital, we are grateful to Dr H M Dunn for permission to report on her patients as part of the study.

REFERENCES

1. Murphy G J J, McAleer J J A, O'Connor F A. Drug overdoses – a three year study at Altnagelvin Hospital, Londonderry. *Ulster Med J* 1984; **53**: 131-139.
2. Proano L, Chiang W K, Wang R Y. Calcium channel blocker overdose. *Am J Emerg Med* 1995; **13**: 444-50.
3. Ramoska E A, Spiller H A, Winter M, Borys D. A one-year evaluation of calcium channel blocker overdoses: toxicity and treatment. *Ann Emerg Med* 1993; **22**: 96-200.
4. Connolly D L, Nettleton M A, Bastow M D. Massive diltiazem overdose. *Am J Cardiol* 1993; **72**: 742-3.
5. Kenny J. Treating overdose with calcium channel blockers – it's their cardiovascular effects that kill. *Br Med J* 1994; **308**: 992-3.
6. DeLima L G R, Kharasch E D, Butler S. Successful pharmocologic treatment of massive atenolol overdose: sequential hemodynamics and plasma atenolol concentrations. *Anaesthesiology* 1995; **83**: 204-7.
7. Greig J, Groden B M. Persistent electrocardiographic changes after flecainide overdose. *Br J Clin Pract* 1995; **490**: 218-9.
8. Bodenhamer J E, Smilkstein M J. Delayed cardiotoxicity following quinine overdose: a case report. *J Emerg Med* 1903; **11**: 279-85.
9. Taboulet P, Band F J, Bismuth C, Vicant E. Acute digitalis intoxication – is pacing still appropriate? *J Toxicol Clin Toxicol* 1993; **31**: 261-73.
10. Bosse G M, Pope T M. Recurrent digoxin overdose and treatment with digoxin-specific Fab antibody fragments. *J Emerg Med* 1994; **12**: 179-85.