arousal seeking behaviour.²⁰ Finally, volunteering parents were motivated by a desire to help others and contribute to medical research, but they were also searching for more information and better ways to help their own children, who were very young and had a distressing chronic illness.

As far as we can determine, there was no selection bias in the recruitment of the non-volunteering parents. The children were of similar age and severity of illness. The two groups of parents were also similar with regard to age, birth order, parity, and ethnic background. A higher proportion of the main decision makers in the volunteering group were women, and it is well known that women use drugs and health services more frequently than men. In addition, there were clear socioeconomic differences between the groups, and it is reasonably well established that social supports and behaviour that risks health are related to social state. The sample size was not large, and the data should therefore be interpreted with some caution. Nevertheless, the finding that volunteering parents were significantly more socially disadvantaged and emotionally vulnerable has important implications in the ethics of recruitment; vulnerable groups such as children, prisoners, students, and the mentally handicapped are generally excluded from clinical trials. The question arises whether current practice needs to be reviewed in the light of our finding that vulnerable parents may be volunteering their vulnerable children for clinical research.

We thank Dr David C Chant, group statistical adviser to the department of social sciences, University of Queensland, for help, advice, and guidance with analysing the data. This work was supported in part by a grant from the Mayne Bequest Fund, University of Queensland.

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(Accepted 20 March 1990)

Association of intravenous erythromycin and potentially fatal ventricular tachycardia with Q-T prolongation (torsades de pointes)

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Br Med J 1990;300:1375-6

Ventricular arrhythmias during treatment with erythromycin are a rare but important side effect.¹ We report a case of potentially lifethreatening ventricular arrhythmias associated with prolongation of the Q-T interval induced by erythromycin.

Case report

A 61 year old woman was admitted with fever, pneumonia, and severe respiratory distress (respiratory rate 40/min, arterial oxygen pressure 7.4 kPa breathing 10 l oxygen/min). She was maintained with phenprocoumon because of longstanding pulmonary hypertension secondary to pulmonary embolism. Examination disclosed tricuspid regurgitation; an enlarged, tender liver; pulse rate 108/min; and blood pressure 125/70 mm Hg. The electrocardiogram showed sinus tachycardia, right atrial hypertrophy, and a normal rate corrected Q-T interval ($Q-T_c$ 410 ms). Results of laboratory investigations were: sedimentation rate 64 mm in first hour; haemoglobin concentration 180 g/l; white cell count $37 \times 10^9/l$ (75% band forms); plasma bilirubin concentration 99 $\mu\text{mol/l}$ (normal <15.4); serum aspartate aminotransferase

activity 95 U/l (normal 6-23). Plasma electrolyte concentrations, including potassium, sodium, calcium, and magnesium, were normal, as was the plasma creatinine concentration. Ceftriaxone (2 g daily) and erythromycin lactobionate (1 g thrice daily infused in saline over 90 minutes) were started. During the fifth infusion of erythromycin pronounced prolongation of the Q-T interval ($Q-T_c$ 550 ms), multiform ventricular extrasystoles, and an episode of non-sustained torsades de pointes occurred.

During the eighth and 10th infusions several electrocardiograms and rhythm strips were recorded, showing increasing $Q-T_c$ intervals during infusion and a gradual return to normal over the subsequent five to six hours (figure). Coinciding with maximal prolongation of the $Q-T_c$ interval again torsades de pointes occurred. Electrolyte and cardiac enzyme values remained normal and an electrocardiogram recorded shortly after the last episode of torsades de pointes showed no signs of myocardial ischaemia. During the periods of

Time course of changes in $Q-T_c$ interval (rate corrected $Q-T$ interval according to Bazett's formula) during two 90 minute infusions of erythromycin

rhythm disorders no other drugs known to prolong the Q-T interval and induce torsades de pointes—for example, diuretics or antiarrhythmics—had been given. Antibiotic treatment was changed to ciprofloxacin. No further arrhythmia occurred and the patient was discharged three weeks later.

Comment

Ventricular arrhythmia associated with prolongation of the Q-T_c interval is a well known side effect of several drugs. In our patient the close temporal relation of prolongation of the Q-T_c interval and infusion of erythromycin with the maximum interval occurring at the end of the infusion and a gradual return to normal over the next few hours strongly suggested a direct dependence of the Q-T_c interval on the plasma concentrations of erythromycin. That we recorded this phenomenon during two separate drug infusions lends support to this suggestion. A possible association of erythromycin with ventricular arrhythmias has been reported.^{1,2} Prolongation of the Q-T interval was the common feature in all cases. Nevertheless, given the widespread use of erythromycin, the low rate of drug associated arrhythmias recognised is remarkable.

In our patient ventricular extrasystoles and torsades de pointes occurred only at the time when peak plasma concentrations would be expected and when the longest Q-T_c interval was seen. How erythromycin alters cardiac repolarisation is not clear, but a recent electrophysiological study has shown that erythromycin exerts a concentration dependent at quinidine-like effect.³ Aside from the mode of administration leading to different peak plasma concentrations other factors must be considered. In patients with pre-existing

prolongation of the Q-T interval—for example, in idiopathic long Q-T syndrome⁴—erythromycin may worsen the repolarisation abnormality and induce arrhythmias. As in other published cases² our patient had a normal Q-T interval before being given the drug. Other factors such as alterations of erythromycin pharmacokinetics resulting in different individual susceptibility may be important. Both structural damage of liver tissue and cotreatment with other drugs competing for the same hepatic cytochrome (P450III_{A4}) may impair hepatic drug clearance and lead to critically raised plasma concentrations of erythromycin.⁵ The hepatic dysfunction present in our patient may have been a main factor contributing to the erythromycin toxicity.

To minimise the danger of toxic plasma concentrations rapid injections of erythromycin should be avoided as recommended by the manufacturers. In patients at risk close Q-T_c and rhythm monitoring may be advisable. In a patient with impaired hepatic drug metabolism or pre-existing cardiac disease a smaller dose or an alternative antibiotic should be considered.

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(Accepted 2 March 1990)

Prolonged recovery of renal function after prostatectomy for prostatic outflow obstruction

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Br Med J 1990;300:1376-7

High pressure chronic retention from prostatic outflow obstruction presents with few urological symptoms, but the presence of late onset enuresis and a painless, palpable bladder, with hypertension or peripheral oedema, should suggest the diagnosis.¹ Progressive renal failure is a feature of this condition, and prostatectomy is essential to relieve obstruction of the lower urinary tract. Prospective tests of renal function done up to one year after prostatectomy show that appreciable improvement may occur.² Further recovery may, however, occur some years later and these observations form the basis of my report.

Patients, methods, and results

Three men, aged 48, 51, and 63, with typical features of high pressure chronic retention associated with prostatic outflow obstruction, were studied prospectively for between three and nine years after prostatectomy.¹ They formed part of a larger series of six patients, one of whom had died of an unrelated cause and two had not yet been followed up for three years.² All six patients showed a consistent improvement in renal function over a period of 12 months, with their mean glomerular filtration rate rising from 27 ml/min/1.73 m² to 56 ml/min/1.73 m² and their mean effective renal plasma flow rising from 88 ml/

min/1.73 m² to 221 ml/min/1.73 m² (p<0.02 for both values). Their mean filtration fraction was 0.30 preoperatively and 0.25 one year after prostatectomy.

All three patients were hypertensive at presentation, but two became permanently normotensive within days of prostatectomy. The third patient experienced resurgence of severe hypertension two months after prostatectomy requiring control with multiple anti-hypertensive drugs.

The figure shows the effective renal plasma flow and glomerular filtration rate for each patient before and after prostatectomy.³

Intravenous urography, renal tract ultrasonography, and gammacamera renography were performed before prostatectomy and at arbitrary intervals after for several years. Initial urography showed gross bilateral hydronephrosis and hydroureter in all three patients, which changed to normal appearances some years after prostatectomy. These findings were confirmed by ultrasonography.

The renographic findings were not diagnostic of obstructive nephropathy before prostatectomy, but they did show bilateral impairment of renal function with poor uptake of isotope. Nevertheless, when renal function had recovered a normal renogram pattern was seen.

Comment

Prognosis in high pressure chronic retention depends on the degree of renal damage at the time of presentation. No test can gauge whether irreversible pathological changes have occurred. Even when renal function is substantially impaired initially, the amount of recovery possible may be established only by surgical relief of the obstruction or by catheterisation