Ahern *et al.*'s (1987) placebo group showed the expected response to placebo, with some degree of improvement. Despite this small improvement the response of the placebo group is none-the-less of considerably smaller magnitude than the response of those patients treated with active drugs after 24 h of treatment.

It can also be seen that the response in Bluestone's (1982) low (20 mg day⁻¹) and high dose (40 mg day⁻¹) groups were little different from the response seen in Ahern *et al.*'s (1987) placebo group. This may reflect the prolonged plasma *t*_{1/2} life of this drug, since effective plasma concentrations may not have been achieved at this early stage in the low dose group. Also of interest is the variability of relief of pain in the trials of active drugs in the initial treatment period.

Also of interest is the variability of relief of pain in the trials of active drugs in the first 24 h of therapy. In particular, the results of Bluestone (1982), Murphy (1979), Ahern *et al.* (1987) and Ruotsi & Vainio (1978) show at best only a 12% improvement over placebo, and a 27% improvement over the untreated group of Bellamy *et al.* (1987). This may reflect factors of patient selection, but may also poorly reflect on the capacity of treatment (in some instances) to achieve the desired result; namely the swift relief of pain.

The other studies with active drugs (Marcolongo *et al.* (1980), and Widmark (1982)) show pronounced differences when compared with Bellamy *et al.*'s (1987) untreated group which are greatest after 24 h of therapy. This confirms the latter authors' conclusions regarding the potential value of using their observations on untreated gouty arthritis patients as a control group for anti-inflammatory drug trials in this disease. Bellamy *et al.*'s (1987) study may be useful as an external control group against which the rapidity of pain relief and time to resolution of the acute attack in further trials of non-steroidal anti-inflammatory drugs in this disease may be assessed.

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Propafenone in the treatment of chronic ventricular arrhythmias in a pregnant patient

Propafenone is widely used in the treatment of chronic ventricular arrhythmias (Harron & Brodgen, 1987) but, so far, no data are available

on the use of this drug during pregnancy (Mitani *et al.*, 1987). We assessed the maternal-foetal transfer of propafenone in a pregnant patient

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with valvular cardiopathy who required this agent for complex ventricular arrhythmias.

A 22 year-old woman, who had suffered frequent streptococcal infections during infancy, was admitted to the hospital for exercise-related syncope. Among other examinations, cineangiography revealed severe mitral insufficiency, moderate aortic insufficiency and a dynamic obstacle to ventricular ejection, with no intra-ventricular pressure gradient at rest.

She was well until 3 years after this when, during the 11th week of pregnancy, she complained of palpitations. An electrocardiogram revealed the presence of rapid atrial fibrillation. Therapy with digoxin 0.25 mg per day was started. Two months later, frequent premature ventricular contractions (PVCs) were present in a standard electrocardiogram. A 24 h Holter monitoring showed atrial fibrillation (heart rate between 35 and 125 beats min^{-1}); a total number of 2748 PVCs, with 166 couplets, five runs of 3 beats and three runs of nonsustained ventricular tachycardia (15, 6 and 4 beats, at a rate of 160–170 beats min^{-1}). Plasma concentrations of K^+ and digoxin at the time of recording were 3.9 mmol l^{-1} and 0.65 ng ml^{-1} respectively.

Therapy with propafenone 150 mg three times daily was started. Holter monitoring showed 1417 PVCs, two couplets, three triplets, and a 4 beats run of ventricular tachycardia. Dosage was raised to 300 mg three times daily. The Holter monitoring during treatment with this dosage showed 146 PVCs (93% reduction compared with baseline); 10 couplets (94% reduction), two triplets (60% reduction) and no runs of ventricular tachycardia. No slowing of atrial fibrillation was observed.

Plasma concentrations of propafenone during chronic treatment with 300 mg three times daily, measured by high pressure liquid chromatography (Latini *et al.*, 1988), ranged between 419 ng ml^{-1} (1 h after drug intake) and 96 ng ml^{-1} (7 h after drug intake) and those of its major active metabolite, 5-OH-propafenone, ranged between 187 and 63 ng ml^{-1} . No significant changes were observed in electrolytes and in plasma concentration of digoxin. Treatment with propafenone continued throughout pregnancy. No side effects occurred. Foetal heart rate was between 135 and 155 beats min^{-1} . At 36 weeks of pregnancy, the patient was admitted to the hospital for caesarean section. No complex arrhythmic events occurred during the intervention. At birth, the neonate weighed 2.450 kg; its Apgar index was 8/10 after 1 min and 10/10 after 5 min and its heart rate was in the normal range. A blood sample drawn from the umbilical cord just after delivery showed a plasma concentration of 21 ng ml^{-1} propafenone and 39 ng ml^{-1} 5-OH-propafenone. At that time, maternal plasma concentrations were 71 ng ml^{-1} and 86 ng ml^{-1} , respectively. Both mother and neonate were well during the days after delivery.

This study found that propafenone and 5-OH-propafenone are both transferred to the foetus, though only to a limited extent (30–40%). The drug, given in the third trimester of pregnancy at the dosage of 300 mg three times daily to treat complex ventricular arrhythmias was not harmful to the foetus. However, administration of propafenone earlier in pregnancy would result in longer foetal exposure and its cardiovascular indexes should be carefully monitored.

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