

SHORT REPORTS

Maternal administration of flecainide to terminate and suppress fetal tachycardia

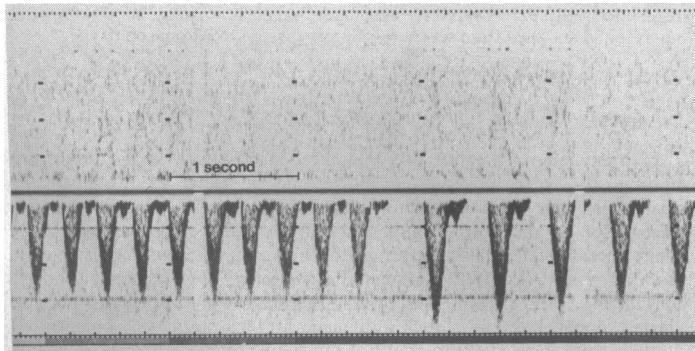
Fetal echocardiography has allowed fetal arrhythmias to be identified and accurately diagnosed. Because a fetal tachycardia is often detected before an elective delivery is safe considerable interest has focused on treatment by giving drugs to the mother. Digoxin is accepted as the drug of first choice, but no consensus exists on second line drugs.^{1,2} We present the first report of giving flecainide to a mother to terminate and suppress a fetal tachycardia.

Case report

A tachycardia was identified during routine auscultation of the fetal heart at 28 weeks' gestation. The echocardiogram showed a ventricular rate of 240 beats/min with a 1:1 atrioventricular relation. The tachycardia was present 95% of the time. The heart was structurally normal, but a moderate pericardial effusion and ascites were noted.

The mother was given oral digoxin 500 µg three times in 24 hours and then 500 µg daily, which resulted in a trough plasma concentration of 1.5 µg/l. Repeat echocardiography over the next 11 days showed persistent tachycardia with no change in the pericardial or ascitic effusions.

At 30 weeks' gestation the mother was admitted to hospital. Three echocardiograms taken on the day of admission confirmed a tachycardia. During echocardiographic monitoring of the fetus the mother was given intravenous flecainide 110 mg (1.4 mg/kg) over five minutes. The fetal ventricular rate slowed from 235 to 214 beats/min and then fell abruptly to 120 beats/min as the tachycardia stopped and sinus rhythm supervened (figure). Sinus rhythm persisted during observation for the next 10 minutes. Oral flecainide 100 mg three times daily was substituted for the digoxin treatment. The fetus remained in sinus rhythm, and the maternal echocardiogram did not change. Echocardiograms taken on four subsequent occasions showed no recurrence of the arrhythmia. All traces of pericardial and ascitic effusion resolved within 10 days. The maternal plasma concentration of flecainide measured once before administration of the drug was 656 µg/l (normal adult therapeutic range 400-1000 µg/l).



Pulsed Doppler recording of blood velocity in fetal ascending aorta during intravenous administration of flecainide to the mother.

Labour was induced at 38 weeks' gestation, and a female baby weighing 3450 g was delivered in good condition. A 12 lead electrocardiogram showed no evidence of pre-excitation. The baby did not receive any drugs, and arrhythmia did not recur during observation for 10 days. Concentrations of flecainide in maternal and cord plasma obtained simultaneously five hours after the last oral dose were 833 and 533 µg/l, respectively.

Comment

Assessment of the effectiveness of treatment of fetal arrhythmias is hampered by lack of knowledge of the natural course of these conditions and the transplacental pharmacokinetics of many drugs and their modification by fetal hydrops. Termination of a fetal tachycardia some days after the start of oral treatment of the mother may be spontaneous rather than drug induced.¹

Digoxin is accepted as the drug of first choice for treating fetal tachycardia^{1,2} but is ineffective in up to half of cases.¹ Reports of treatment with other drugs are few, but tachycardia has been terminated with propranolol, verapamil, procainamide, and amiodarone.^{1,2} Verapamil is not recommended for neonatal tachycardia, and its use in fetal hydrops may be associated with fetal or neonatal death.¹

Flecainide was chosen in this case because it is known to be safe and effective in various types of arrhythmias in children.³ Although its transplacental pharmacokinetics are not known, its molecular weight (474.4 daltons) suggests that it should cross the placenta easily.⁴ The rapid termination of the tachycardia confirmed its efficacy and justified oral administration to the mother to prevent recurrence. Further experience is needed, however, to compare flecainide with other drugs before it can be recommended for treating fetal tachycardia.

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High dose intravenous methylprednisolone or high dose intravenous gammaglobulin for autoimmune thrombocytopenia

Since the initial report of Imbach *et al* high dose intravenous gammaglobulin has become a popular treatment for autoimmune thrombocytopenia.¹ It is effective, induces a quick rise in the platelet count, and rapidly diminishes bleeding; moreover, it has no appreciable side effects.^{2,3} It seems to be the treatment of choice in patients with an active bleeding tendency ("wet purpura"), but it is expensive.

Intravenous gammaglobulin probably works by transient inhibition of autoantibody mediated platelet destruction by the cells of the macrophage system (at the level of IgG Fc receptors), although other mechanisms have been postulated as well.² Glucocorticosteroids also inhibit the destruction of autoantibody sensitised platelets by the cells of the macrophage system.⁴ From experience with the treatment of organ graft rejection high doses of intravenous corticosteroids are also known to be rapidly effective. When given only for a few days they have no serious side effects, and are not so expensive as gammaglobulin. Hence we studied the effect of high dose intravenous methylprednisolone in treating patients with autoimmune thrombocytopenia, comparing it with intravenous gammaglobulin and oral prednisolone.

Patients, methods, and results

The patients were adults with their first attack of idiopathic autoimmune thrombocytopenia. Some were treated again for a relapse, after having no treatment (oral prednisolone) for over three months. Bone marrow appearances were normal, with a normal or increased number of megakaryocytes and a positive immunofluorescence test for platelet autoantibodies. Other causes for thrombocytopenia were excluded. Ten patients were treated with one course of intravenous methylprednisolone (1000 mg) given over half an hour for three consecutive days. Twelve other patients were treated once and two twice with intravenous gammaglobulin (from the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service⁵) 0.4 g/kg for five days. A dose of 20 mg prednisolone was started after this initial treatment. Platelet counts were determined daily or every other day by standard methods. Of a control series of 17 patients 14 were treated once and three twice with oral prednisolone, 40-80 mg daily, given in three to four doses per day.

Intravenous methylprednisolone was as effective as intravenous gammaglobulin in terms of the frequency of response. The proportion of patients who obtained an adequate platelet count ($>50 \times 10^9/l$) within 10 days was 80% (8 out of

10 courses) and 81% (13 out of 16 courses) respectively. There were no side effects. Oral prednisolone was initially less effective (70% response) but roughly the same proportion of patients (85% or 16 out of 20 courses) reacted within three to four weeks, the delay being due to a slow response in three patients. The table shows the mean platelet counts in the three patient groups for those patients who reacted to treatment. The effect of intravenous corticosteroids was even faster than that of intravenous gammaglobulin, although the difference was not statistically significant.

Platelet count ($\times 10^9/l$; mean (SD)) before and during treatment and with maintenance treatment

Drug	Day				
	0	3	5	7	10
Prednisolone	13 (14)	56 (31)	100 (42)	140 (64)	147 (47)
Methylprednisolone	20 (17)	100 (46)	146 (51)	158 (68)	120 (54)
Gammaglobulin	23 (13)	69 (74)	136 (44)	177 (149)	133 (51)

Comment

Our study shows that high dose intravenous methylprednisolone is as effective as intravenous gammaglobulin in treating autoimmune thrombocytopenia; hence it may be considered a less expensive alternative. The effect of intravenous corticosteroids was transient in all our patients, as was that of intravenous gammaglobulin.⁵ Maintenance treatment with a low oral dose of prednisolone (20-40 mg/day) was necessary to ensure a more lasting effect. In the long term oral prednisolone was as effective as intravenously administered corticosteroids. Hence this treatment is indicated only in patients with a severe bleeding tendency. It may also be used to prepare these patients for surgery.

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Antenatal factors associated with obstruction of the gastrointestinal tract by meconium

Obstruction of the gastrointestinal tract by meconium in the neonate ranges in severity from the inspissated meconium syndrome, which may require an operation, to the meconium plug syndrome, which is a failure to pass meconium within the first 24 hours of life and which resolves spontaneously.¹ To identify the factors associated with the condition we examined the antenatal records of eight successive babies who were diagnosed as having meconium obstruction in the neonatal period.

Patients and results

Obstruction of the gastrointestinal tract by meconium was diagnosed in only eight of 400 infants treated in the neonatal intensive care unit at this hospital over

12 months. All eight infants (six girls and two boys) had birth weights that were below the third centile. The mothers had been referred to this hospital at 24-30 weeks' gestation for assessment of severe intrauterine growth retardation.

The fetuses were physically and chromosomally normal; screens for toxoplasma, rubella, cytomegalovirus, herpes, and autoantibodies gave negative results. Abdominal circumferences were below the fifth centile of the normal range for gestation. Each fetus had a hyperechogenic bowel, defined as a mass with a similar echogenicity to the skeleton in the lower half of the abdomen between the liver and the bladder; each fetus also had oligohydramnios, as defined previously.² Doppler ultrasonography showed that the resistance index of the uteroplacental circulation was greater than the 95th centile of the normal range and that the mean velocity of blood in the fetal thoracic aorta was less than the fifth centile; end diastolic frequencies in the umbilical artery were absent.³ Fetal oxygen tension was less than the fifth centile of the normal range for gestation.⁴ The table shows the indications for delivery, the modes of delivery, and the birth weights.

Data on delivery of fetuses with hyperechogenic bowel

Case No	Gestation at delivery (weeks)	Indication for delivery	Mode of delivery	Birth weight (g)
1	30	Hypertension induced by pregnancy	Caesarean section	950
2	35	Premature labour	Caesarean section	960
3	27	Abnormal biophysical profile	Caesarean section	540
4	28	Abnormal biophysical profile	Caesarean section	520
5	28	Abnormal biophysical profile	Caesarean section	680
6	27	Abnormal biophysical profile	Caesarean section	540
7	34	Hypertension induced by pregnancy	Caesarean section	1700
8	30	Premature labour	Caesarean section	450

None of the babies passed meconium in the first 24 hours of life. In six babies the abdomen became progressively distended. This resolved in four (cases 1-4) after spontaneous passage of a meconium plug two to four days after birth. In two babies (cases 5 and 6) the distension did not respond to repeated saline enemas and the obstruction was relieved only after an ileostomy was fashioned. In case 5 recovery was uncomplicated and the ileostomy was closed on day 40, but in case 6 the baby died at the age of three months from septicaemia after the ileostomy was closed. In the two remaining babies (cases 7 and 8) the bowel obstruction was treated with repeated enemas with iohexol from day 3 after birth; one (case 7) responded well and recovered after passage of a meconium plug, but the other did not respond and died from severe respiratory distress syndrome on day 8.

Comment

In pregnancies in which uteroplacental insufficiency is diagnosed the finding of a hyperechogenic fetal bowel may be useful as an indicator of obstruction due to meconium. Meconium is a rare cause of neonatal obstruction of the bowel compared with conditions such as congenital malformations of the gastrointestinal tract and paralytic ileus associated with respiratory distress. Hence antenatal detection of hyperechogenic bowel may allow a correct diagnosis to be made earlier and specific treatment to be started sooner, possibly reducing the need for laparotomies. A prospective study is being carried out to establish the value of hyperechogenic bowel in predicting obstruction due to meconium.

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