CONGENITAL HEART DISEASE

Response to bosentan in children with pulmonary hypertension

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Heart 2006;**92**:664–670. doi: 10.1136/hrt.2005.072314

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Accepted 19 September 2005
Published Online First 10 October 2005

Objective: To describe an early experience of treating 40 children with the dual endothelin receptor antagonist bosentan, which is known to be safe and effective in adults with pulmonary hypertension (PH).
Design: In this retrospective, observational study the UK Service for Pulmonary Hypertension for children treated 40 children with bosentan, 20 with idiopathic pulmonary arterial hypertension (IPAH) (mean age 8.03 years, range 1.2–17) and 20 with PH associated with other conditions (congenital heart disease, parenchymal lung or connective tissue disease, or HIV). Their mean age was 8.3 years (range 0.6–16 years).
Patients: 39 patients were in World Health Organization (WHO) class III and IV, and all had shown recent deterioration. In IPAH the mean pulmonary vascular resistance (PVR) was 21.7 units·m^2 (range 5.6–42.8). In secondary PH the mean PVR was 18 units·m^2 (range 4.9–49). No child had a positive response to vasodilator testing with nitric oxide.
Interventions: Bosentan was given as first line treatment to 25. Nine were given intravenous epoprostenol. Children were treated for a mean of 12.7 months (range 2–24 months).
Main outcome measures: Response to treatment was judged by WHO functional class, six minute walk test, weight, ECG and echocardiographic findings, and need to add additional treatment.
Results: Bosentan was well tolerated. In the IPAH group 19 (95%) stabilised with bosentan treatment but 12 (60%) patients needed combined treatment with epoprostenol. In secondary PH, WHO class, six minute walk test, and weight gain improved significantly.
Conclusion: Bosentan helped stabilise children with IPAH but intravenous epoprostenol was also needed by 60%. Children with secondary PH improved.

Pulmonary hypertension (PH) is a debilitating disease characterised by an increase in pulmonary vascular resistance (PVR) leading to progressive deterioration, right ventricular failure, and death. Sporadic pulmonary arterial hypertension (PAH) with no apparent aetiology is called idiopathic PAH (IPAH).[1] PH in childhood that is not IPAH is usually caused by congenital abnormalities of the heart or parenchymal lung disease and less commonly by connective tissue and other diseases.[2] In the World Health Organization classification (Second World Symposium on Pulmonary Hypertension, Evian, 1998) ''secondary pulmonary hypertension'' was abandoned in favour of a more precise anatomical and functional definition. But the term has been used in the present study as a means of discussing a group of pulmonary hypertensive children with disparate underlying disorders.

Treatment options are more limited in children than in adults. Only a small proportion of the children presenting to the UK Service for Children with Pulmonary Hypertension have been suitable for treatment with oral calcium channel antagonists. For other children the only drug of proven efficacy is epoprostenol, given as a continuous intravenous infusion with all the disadvantages that this entails.[1 3] The introduction of the endothelin receptor antagonist bosentan offered a much needed alternative oral treatment.

Endothelin appears to be important in the pathogenesis of PAH.[4–6] Its actions are mediated by two receptors, endothelin A and endothelin B. The dual endothelial receptor antagonist bosentan diminishes or abrogates endothelin induced smooth muscle cell contraction, hypertrophy and hyperplasia, and fibrosis and reduces both the haemodynamic and structural response to experimentally induced PH.[7 8] In 2002 bosentan was shown to be safe and efficacious in the treatment of adults with PAH and benefit is generally sustained for at least one year.[9–11] Derangement of liver function (rise of hepatic aminotransferase concentration) was the most common side effect. A later study showed that the drug was safe for children to use and that it had a safety profile similar to that in adults.[12] In the present study we report our early experience of treating 40 children with bosentan (Tracleer; Actelion). They were referred to the UK Service for Pulmonary Hypertension.

METHODS

The patient population

Forty children with PAH were treated with bosentan. All were in WHO functional class III and IV except one patient with IPAH who had been treated with intravenous epoprostenol for five years after a cardiac arrest and was now in class II. Twenty patients had IPAH and 20 had secondary PH (tables 1–3). All the children had recently deteriorated notably and had poor exercise tolerance. The older children had stopped attending school. Three children with IPAH had had syncopal attacks. Three children with chronic lung disease were oxygen dependant. The mean age at the start of treatment was 8.03 years for IPAH and 8.3 years for secondary PH. There was a female predominance in IPAH but not in secondary PH. Table 1 presents medications the children were receiving when they started receiving bosentan. Seven children with IPAH and two with secondary PH were receiving intravenous epoprostenol and deteriorating on a mean dose 39 ng/kg/min when treatment with bosentan

Abbreviations: IPAH, idiopathic pulmonary arterial hypertension; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; WHO, World Health Organization

Table 1 Summary of patient demographics and baseline characteristics

	Idiopathic PAH (n = 20)	Secondary PH (n = 20)
Age at treatment (years)		
Mean	8.03	8.3
Range	1.2–17	0.6–16
Boys:girls	5:15	9:11
Ethnicity		
White	19	18
Afro-Caribbean	0	2
Asian	1	0
Weight (kg)	27.5 (8–70)	23.9 (6.8–59.3)
WHO functional class		
II	1	0
III	11	13
IV	8	7
ECG findings		
Sinus rhythm	20	18*
Right axis deviation	20	14†
RV hypertrophy with strain	15	9
Echocardiography		
Tricuspid jet velocity (m/s)	4.6	4.14
Poor RV function	12	5
Atrial communication	11	5
Cardiac catheterisation		
PAP>SAP	9	3
PAP = SAP	7	7
PAP<SAP	4	8
PVR (units·m^2)	21.7 (5.6–42.8)	18.0 (4.9–49)‡
Treatment at start of study		
Nocturnal oxygen	20	20
Diuretics	5	6
Nifedipine	0	4§
Sildenafil	2	4
Epoprostenol	7	2
Anticoagulation	12¶	2
Duration of treatment (months)	13.1 (3–24)	12.2 (2–22)

*One junctional rhythm, one paced; †five superior axis, one paced; ‡n = 18; §three patients had systemic hypertension associated with connective tissue disease; ¶six aspirin, six warfarin.
PAH, pulmonary arterial hypertension; PAP, pulmonary arterial pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RV, right ventricular; SAP, systemic arterial pressure; WHO, World Health Organization.

was started. Table 1 summarises the ECG and transthoracic echocardiographic findings.

In the group with IPAH signs of right atrial and right ventricular hypertrophy were invariably present on the ECG, and 75% of patients had an RV strain pattern. Echocardiography showed right ventricular hypertrophy in all children and systolic function was impaired in 60%. A tricuspid regurgitant jet was invariably present and the velocity exceeded 4 m/s in 95% of children. Pulmonary regurgitation was present in 52%.

An atrial communication was present in 55% of children, either a patent foramen ovale, secundum atrial septal defect, or atrial septostomy. Five children had had a septostomy, including one done for recurrent syncope at the time bosentan was introduced. At cardiac catheterisation (tables 1 and 2), the pulmonary arterial pressure was similar to the systemic arterial pressure or higher in most children. The mean PVR, measuring oxygen consumption, was between 5.6 and 42.8 units·m^2 (mean 21.7 units·m^2). Ten children were aged 5 years or less and the PVR in this group was as great as that in the older children (23.26 *v* 20.22 units·m^2) The six children in WHO class III and IV already being treated with epoprostenol had a mean PVR of 28.7 units·m^2, which was not significantly different from that of the rest of the group. Pulmonary vascular reactivity was assessed by the response to an increase in inspired oxygen concentration and administration of inhaled nitric oxide. No child had a positive response.

In the group with secondary PH ECG showed signs of hypertrophy in the subpulmonary ventricle, with a strain pattern in 45% of all patients. Echocardiography showed hypertrophy of the subpulmonary ventricle in all and impaired systolic function in 60% of the children. A tricuspid regurgitant jet was invariably present, with a velocity exceeding 4 m/s in 95% of children. Pulmonary regurgitation was present in 52%. At cardiac catheterisation (tables 1 and 3), all patients had severe PH and the mean PVR was 18 units·m^2 (range 4.9–49 units·m^2). No child had a positive vasodilator response.

Treatment and follow up

Children were treated for a mean of 12.7 months (range 2–24 months). They were given bosentan orally and dosed according to body weight: < 10 kg, 15 mg twice daily; 10–20 kg, 31.25 mg twice daily; 20–40 kg, 62.5 mg twice daily; > 40 kg, 125 mg twice daily.[12] Liver function tests and a full blood count were carried out before treatment was started and at monthly intervals thereafter.

Treatment was initiated in hospital for the first few days at half the target dose and the systemic arterial blood pressure and vital signs were monitored. The target dose was achieved within a month. All continued to receive nocturnal oxygen and other medications except calcium channel blockers. Eight were anticoagulated with warfarin (table 1). Children were evaluated on an outpatient basis at 1–2 monthly intervals or less. They were assessed for change in WHO class, weight, physical activity, and stabilisation of the clinical condition as indicated by improved well being and a return to school or preschool. The children aged 5.5 years or more did a six minute walk test at every outpatient visit. The ECG and echocardiography findings were also assessed. Clinical deterioration necessitated the addition of intravenous epoprostenol.

Statistical analysis

We compared the percentage improvement in six minute exercise from the pretreatment baseline to the current post-treatment evaluation by using a one sample *t* test and the mean difference in distance by paired *t* test. The standard deviation score of the weight (matched to chronological age and sex) was calculated for both the baseline and end point and values were then compared by paired *t* test. The percentage weight gain and the percentage improvement in the exercise test were correlated with PVR. The Wilcoxon matched paired test was used to calculate the significance of changes in WHO classification before and after treatment.

RESULTS

The drug was well tolerated by all patients, including those receiving simultaneous epoprostenol. Liver function tests remained within normal limits in all but one patient who had slightly increased aspartate aminotransferase to less than twice the upper limit of normal. The other adverse effects previously noted in a small proportion of adult patients receiving bosentan, including headache, dizziness, cough, dyspnoea, and flushing, were not encountered in the children.[10] The study included four patients with Eisenmenger's syndrome and none of these patients experienced a significant fall in systemic arterial oxygen saturation. The ECG and echocardiographic findings did not change significantly in any patient during the course of the study. The children have not been recatheterised.

Outcome in children with IPAH

Of the 11 children receiving bosentan as sole treatment, five subsequently needed to be given epoprostenol in addition to bosentan (table 2). All were 5 years old or less. Three of the

Table 2 Idiopathic PAH clinical summary

Patient	Sex	Age (years)	Mean PAP (mm Hg)	PVR (units·m^2)	Pre-epo	Treatment duration (months)	Epo added	WHO class		Six minutes walk		Weight (kg)	
								Baseline	Change with bosentan	Baseline	% Change with bosentan	Baseline	% Change with bosentan
1(died)	F	1.2	31	12.3	No	4	No	IV				8	2.5
2	M	1.2	91	23.9	No	10	No	III	0			8.5	18
3	F	2.3	71	33	No	20	Yes	IV	0			12.8	14
4	M	2.7	89	38.9	Yes	15	No	IV	−1			9	33
5	F	3.4	74	18.6	No	19	No	III	0			10.3	30
6	F	3.9	65	42.8	No	14	Yes	III	1			16.3	3
7	F	4.1	25	12	No	11	Yes	III	1			14.3	10.4
8	M	4.3	54	13.5	No	18	Yes	IV	0			17.4	4
9	F	5.4	50	14.6	No	22	No	III	0			17.4	19
10	F	5.5	71	23	No	18	Yes	IV	0			15.7	28
11	M	7.2	66	18.6	Yes	3	No	III	−1	262	−14	20.9	−3.3
12	F	7.8	68	30	Yes	11	No	III	−1	180	83	17.1	−2.9
13	M	9.75	59	18.5	Yes	21	No	III	0	315	−1.9	28.8	13.8
14	F	12.4	68	16.1	No	7	No	III	0	334	−43	31	−2.5
15	F	12.5	61	16.9	No	11	No	III	−1	250	92	57.5	12.8
16	F	13.7	49	18	No	4	No	IV	−1	430	−2.3	55	1.8
17	F	14.6	25	5.6	Yes	9	No	II	0	300	21.3	52.6	−7.4
18	F	15.5	51	12.5	No	12	No	III	−1	140	157	51.3	−2.1
19	F	16.2	88	27	Yes	24	No	IV	−1	80	275	36.9	19
20	F	17	73	39	Yes	10	No	IV	−1	160	−0.6	70	−1.1

F, female; M, male; pre-epo, receiving epoprostenol before treatment with bosentan.

five children initially improved on bosentan, two returning to school, but all five eventually deteriorated clinically and treatment with epoprostenol was started after a mean of four months (range 2–6 months).One of these children also had an atrial septostomy for recurrent syncope. One child died suddenly after three months' treatment (patient 1). Thus, only five of 11 patients continued to receive bosentan as sole treatment.

At the time treatment with bosentan was started, seven of 20 patients were already receiving epoprostenol. After the addition of bosentan, six improved clinically and one has been taken off epoprostenol (patient 17). Two of the 20 patients (2 and 16) receiving sildenafil before starting bosentan also improved with the addition of bosentan.

All but one patient were in WHO class III and IV at the start of treatment. A score shift indicated improvement in eight patients but overall classification did not change significantly ($p = 0.1$) (fig 1). The 10 older children performed a six minute walk test. The mean distance walked was 245 m (range 80–430 m). The group improved by a mean of 68 m (95% confidence interval 25 to 161 m), a 57% improvement, which was not significant. Five of the 10 children did, however, improve substantially in exercise capacity (mean improvement 176.8 m) (table 2, fig 1). Of these 20 patients, before treatment six were below normal weight for age and sex and 14 were within two standard deviations of the normal. These relations did not change with treatment ($p = 0.55$). Of the older 10 patients only four gained weight and the mean gain was only 3%. In the 10 younger patients in whom weight gain was taken as a marker of improvement, mean weight improved by 2.15 kg ($p = 0.01$), a mean gain of 16%. Improvement in neither weight nor six minute walk test correlated with PVR.

In summary, in the group with IPAH all children were deteriorating clinically when treatment with bosentan was started and all except one were stabilised (table 2).

Outcome in children with secondary PH

Of the 14 patients given bosentan as sole treatment, only the patient with HIV subsequently needed the addition of epoprostenol (patient 20). At the time treatment with bosentan was started two patients (11 and 16) were already being treated with epoprostenol. Both have improved and one has been taken off epoprostenol. Four other patients were already receiving sildenafil. The three children with chronic lung disease were no longer oxygen dependant throughout the 24 hours. All patients were in WHO class III and IV at the start of treatment and there was a significant improvement ($p = 0.001$) (fig 1). None deteriorated and the score shift indicated improvement in 11.

Eleven older patients performed a six minute walk test before and after treatment, and 10 improved on treatment. The 11 children attained a mean increase in distance of 128.2 m (20–300 m) (table 3, fig 1). The mean percentage improvement of 80% was significant ($p = 0.002$). With bosentan treatment weight increased in all but one of the 20 children, the mean increase being 14.25%. Before treatment 10 of the children were below the normal weight for age and sex and the remainder were within two standard deviations; these relations did not change with treatment (paired t test $p = 0.38$). Clinical response was judged by weight alone in the children too young to do a six minute walk test. The nine young children gained weight by a mean of 17.5% ($p = 0.01$). Neither the improvement in exercise performance in the older children nor the weight gain in the young children correlated with baseline PVR.

In summary, all of the children with secondary PH were deteriorating at the onset of treatment and WHO class improved significantly after bosentan treatment. In addition, the older ones improved significantly in the six minute walk test and the younger ones gained significant weight. The number of patients with heart or lung disease was too small to permit subgroup analysis.

DISCUSSION

This observational study reporting our experience of treating 40 children with severe, symptomatic PAH with bosentan is encouraging. The drug was given as first line treatment to 25 children and to another 15 who were deteriorating on their existing treatment. Six children did not maintain improvement with bosentan treatment and another specific treatment was added. With or without an additional treatment, of 20 children with IPAH 19 achieved stabilisation and clinical benefit and in 20 children with secondary PH there was objective evidence of clinical improvement. The drug was well tolerated by all patients, including those with Eisenmenger's syndrome. The major limitation of this study is the relatively small number of children treated, making analysis of outcome impossible with respect to disease aetiology in children with secondary PH.

It was encouraging that 20 children with IPAH achieved stability and even some improvement, given the appalling prognosis in this disease.[3 13] The mean PVR at the start of treatment was higher in the present study than the baseline resistance reported in previous trials of bosentan in adults.[10 14] Finding that the resistance was as high in children < 5 years of age as in the older children indicates the aggressive nature of the disease in the very young and supports the contention that the resistance is high from birth in some patients. After treatment, however, we found that the mean distance walked in six minutes by the 10 older children had not decreased with time and the weight of the younger children had not decreased; in fact, both had increased. Nor had the ECG or echocardiographic findings deteriorated any further. Among the 11 children given bosentan as first line treatment five remained well with bosentan monotherapy. In a large recent adult study 85% of patients in WHO class III and IV remained alive and well with bosentan monotherapy at one year.[15] Five of our other patients improved initially, deteriorated after a mean of four months, and sustained the improvement after the addition of intravenous epoprostenol. We noticed that the children could deteriorate suddenly and unexpectedly and they were all monitored closely. The variability in response presumably reflects the state of disease at the onset of treatment and varying rates of disease progression. The findings in this small study are similar to those in an adult study of 169 patients in which the Kaplan-Meier estimate of survival at one year was 96% for patients given bosentan as first line treatment with the later addition of other specific treatments as indicated.[15]

Seven children with IPAH deteriorating when taking what were considered to be adequate doses of epoprostenol improved when given bosentan. Children tolerate and indeed need higher doses of epoprostenol than adults but, since aggressive uptitration in adults can lead to high output cardiac failure, we tried to avoid this complication in our paediatric patients.[16] Pharmacokinetic interaction is unlikely, since the drugs have different metabolic and excretory pathways and the pharmacokinetics of bosentan are not affected by concomitant treatment with epoprostenol.[12 17 18] One patient with a PVR of 5.6 units·m^2 during long term treatment with low dose epoprostenol was taken off the drug as has previously been reported.[19 20]

Thus, treatment with bosentan was beneficial in 95% of the children with IPAH, but combined treatment with epoprostenol was necessary in 60% of patients. A better outcome might have been achieved had the drugs been given

Table 3 Secondary PH clinical summary

Patient	Sex	Age (years)	Diagnosis	Mean PAP (mm Hg)	PVR (units·m^2)	Treatment duration (months)	WHO class		Six minutes walk		Weight (kg)	
							Baseline	Change	Baseline	% Change	Baseline	% Change
1	F	1.7	AVSD (E)	57	12	22	III	−1			8.7	18
2	M	2.7	TGA/Rastelli	37	36.1	22	IV	0			10	55
3	F	4.2	AVSD, po	38	4.9	16	III	−1	240	76	15.3	16
4	F	4.3	AVSD, po	–	20	7	III	0			15	11
5	M	5.8	TGA, VSD Switch	57	9.4	12	III	−1	110	183.5	13.4	6.7
6	F	10.1	AVSD (E)	83	36.9	17	III	0	80	125	27.9	12
7	F	11.3	TA,VSD (E)†	38	18.7	11	IV	−1	210	24.5	18.5	19
8	M	14.2	TAPVD, po	53	13.3	19	IV	−1	310	36	25.8	9.26
9	M	14.3	TGA/Senning	51	8.1	18	III	−1	290	82	59.3	17
10	M	15.1	DORV (E)	72	17.3	11	III	0	80	127.5	44.1	7.5
11*	F	15.2	TGA/Senning	53	18.4	16	IV	−1	160	187.5	42.1	7.7
12	F	15.7	pAVSD, po	49	13.2	7	III	0	400	7.5	31	4.5
13	F	0.6	CLD	–	–	2	IV	0			6.8	25
14	F	1.9	CLD	32	10.1	19	III	−1			9.3	0
15	M	2.4	CLD	78	49	12	III	−1			12	29
16*	M	3.3	Systemic sclerosis + SAH	43	8	8	III	0			9.6	−6.7
17	M	7.3	Diffuse interstitial lung disease + SAH	48	19.1	6	IV	0			33.5	7.2
18	M	8.1	Cutis marmorata	43	8.25	5	III	−1	312	33.3	19.9	22.4
19	F	12.25	CT disorder/pulmonary fibrosis + SAH	–	–	9	IV	−1			32.8	19.6
20	F	16	HIV	80	22.1	6	III	0	340	−5.8	44.4	4.95

*Taking epoprostenol at start; †repaired truncus arteriosus with interrupted left pulmonary artery and residual ventricular septal defect (VSD).
AVSD, atrioventricular septal defect; CLD, chronic lung disease; CT, connective tissue; DORV, double outlet right ventricle; E, Eisenmenger's syndrome; pAVSD, partial atrioventricular septal defect; po, postoperative; SAH, systemic arterial hypertension; TA, truncus arteriosus; TAPVD, total anomalous pulmonary venous drainage; TGA, transposition of the great arteries.

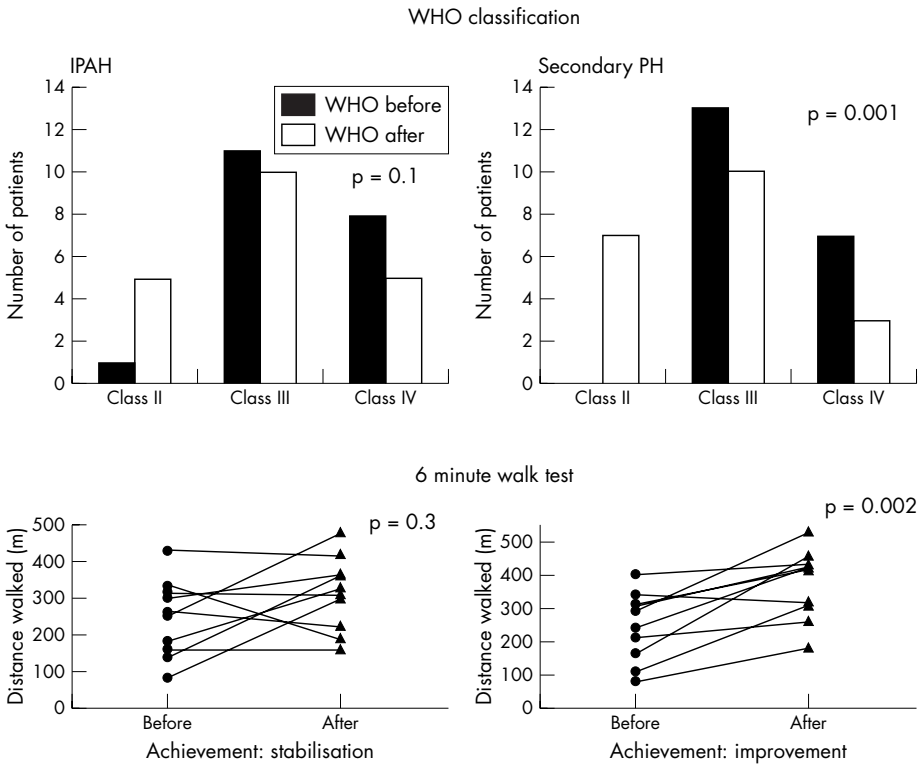

Figure 1 World Health Organization (WHO) classification and results of the six minute walk test before and after treatment with bosentan in patients with idiopathic pulmonary arterial hypertension (IPAH) and secondary pulmonary hypertension (PH).

simultaneously from the beginning, particularly as we were treating children, in whom the pulmonary vasculature is remodelling rapidly even in the normal child. In a recent small adult study lasting 16 weeks those receiving both treatments tended to have a greater clinical and haemodynamic benefit but the trend did not reach significance.[21]

In children with secondary PH bosentan produced a significant improvement in WHO class, exercise capacity as reflected in the six minute walk test, and weight gain. Eight children with congenital heart disease had had a technically successful intracardiac repair. Acceleration of pulmonary vascular disease after cardiac repair is well recognised and the children in the present study were deteriorating rapidly until treatment with bosentan was started. Given the similarities in pulmonary vascular pathology it is logical to offer them the same treatment as children with IPAH are given. One child was already being treated with epoprostenol, known to achieve clinical and haemodynamic improvement in such patients, but was deteriorating until he was also treated with bosentan.[3] Four children had Eisenmenger's syndrome and showed evidence of clinical improvement after treatment, with no deleterious effects such as a fall in systemic arterial pressure or arterial oxygen saturation. The six minute walk test showed an improvement in the distance walked in the three children old enough to do the test as it did in the 10 adults with Eisenmenger's syndrome recently reported by Gatzoulis *et al*.[22] Three severely symptomatic children had chronic lung disease and three children with connective tissue disease also had pulmonary fibrosis. After treatment with bosentan four of these six children had a beneficial shift in WHO class, their oxygen requirements decreased, and one child with systemic sclerosis was taken off epoprostenol. The patient with HIV improved initially with bosentan treatment but it became necessary to add epoprostenol. Both drugs are efficacious in adults with HIV.[23 24] Four children received sildenafil in addition to bosentan, before it was shown that bosentan decreases the plasma concentration of sildenafil.[25]

In assessing the response to bosentan several issues that are specific to children need to be considered. In most adult trials of bosentan exercise capacity as reflected in the six minute walk test has been taken as the primary end point, but its use is obviously restricted by age. It has been shown to be reliable in children and was previously found to be reliable in children with PH aged 7 years and older.[20 26 27] Nor is quality of life assessment as straightforward as it is in adults, reflecting as it does an indirect assessment of how the child is feeling. We found weight to be particularly useful as an indicator of response and well being in young children. In the present study the ECG and echocardiogram were helpful in that we did not find evidence of deterioration in cardiac performance but they gave us no indication as to how bosentan might have improved performance, if at all.

Conclusion

In the present study, bosentan stabilised and improved the clinical condition of children with IPAH although combination treatment with intravenous epoprostenol was necessary in 60% of patients. Significant benefit was achieved with bosentan as a monotherapy in a group of children with severe secondary PH. Larger studies are needed to establish criteria for selecting the most appropriate treatment for first line treatment of each child and to find out whether giving a combination of bosentan and epoprostenol to children at the onset of treatment is advantageous to achieve maximum early benefit.

ACKNOWLEDGEMENTS

The authors thank very sincerely all the UK paediatric cardiologists and paediatricians who referred and helped care for these children as part of the UK Pulmonary Hypertension Service for Children. They also thank Dr Simon Gibbs for his helpful comments on the manuscript.

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Competing interest statement: Professor S G Haworth is a consultant to Actelion Pharmaceuticals. Dr A A Hislop receives some financial support from the same company, and Dr S Maiya and Yvette Flynn have received reimbursement for attending scientific meetings from the same company.

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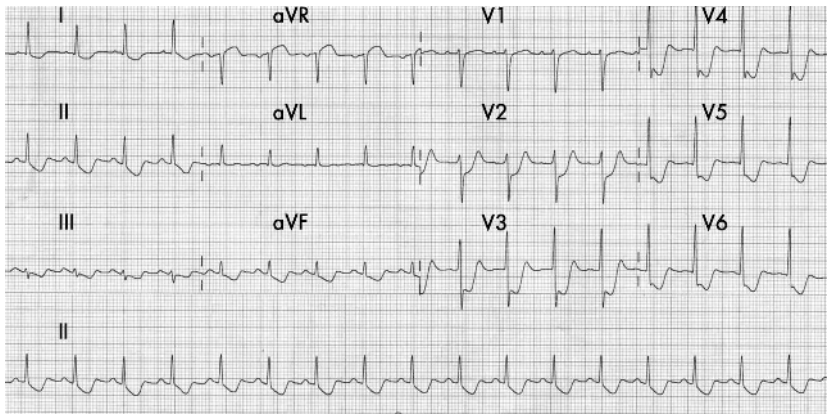
IMAGES IN CARDIOLOGY

doi: 10.1136/hrt.2005.075416

ECG showing features of total left main coronary artery occlusion

A 54 year old man was admitted to our hospital with recent onset anginal chest pain. His ECG at the time of admission (panel) showed pronounced diffuse ST segment depression in leads V2–V6, I, aVL, II and aVF. It also showed ST segment elevation measuring 2 mm in the lead aVR and measuring 1 mm in lead V1. His creatine phosphokinase MB concentration was 164 IU/dl. A bedside troponin T test was positive. He was regarded as being at high risk of acute coronary syndrome (ACS) and was treated with upstream eptifibatide infusion and an early invasive strategy. Coronary angiogram done subsequently showed 100% occlusion of the left main coronary artery. The patient was subjected to emergency coronary bypass surgery.

This ECG illustrates the features of left main coronary occlusion in the form of ST elevation in lead aVR (2 mm) > ST elevation in lead V1 (1 mm). Lead aVR ST segment elevation greater than the V1 ST segment elevation can predict left main stenosis in patients with ACS, and its early recognition can improve clinical outcomes in these patients. Another notable feature is the diffuse ST depression in nine of the 12 leads, suggesting a very severe circumferential ischaemia and a possible left main coronary occlusion. This ECG illustrates the utility of lead aVR in achieving a diagnosis and planning a treatment strategy for these patients.



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