Use of esmolol in a parturient with hypertrophic obstructive cardiomyopathy

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Summary
The physiological changes occurring during pregnancy and labour may reveal or exacerbate the symptoms of hypertrophic obstructive cardiomyopathy (HOCM). We describe the management of labour in a patient with severe HOCM during which esmolol, a short-acting β adrenergic antagonist, was used together with extradural analgesia and invasive cardiovascular monitoring to achieve an assisted vaginal delivery with minimal haemodynamic disturbance. The effects on the infant are described and the literature on the use of esmolol in pregnancy is reviewed. (Br. J. Anaesth. 1995; 75: 801–804)

Key words

Case report
A 29-yr-old primigravid Asian woman presented in the antenatal booking clinic, where the presence of an asymptomatic systolic murmur known to have been present since childhood was confirmed. She was referred for cardiological assessment. An echocardiogram performed at 17 weeks’ gestation revealed severe concentric left ventricular hypertrophy, abnormal aortic valve motion with early closure and a peak systolic gradient of 50 mm Hg. A diagnosis of severe hypertrophic obstructive cardiomyopathy was made. She remained asymptomatic until 33 weeks’ gestation when she was admitted from the antenatal clinic complaining of recent onset of shortness of breath and increasing fatigue. Clinical examination and a chest x-ray revealed pulmonary oedema. Repeat echocardiography revealed worsening left ventricular outflow obstruction with a peak aortoventricular gradient of 80 mm Hg. She was treated with oral diuretics and bed rest. Despite advice emphasizing the potential gravity of her condition, she was unwilling to remain in hospital but agreed to return immediately should any adverse symptoms occur, or at the first sign of the onset of labour. She was reviewed at weekly intervals for the remainder of her pregnancy.

She remained asymptomatic, receiving oral diuretic therapy, and, despite earlier advice, presented at 39 weeks’ gestation with a history of spontaneous rupture of membranes 18 h previously and 2 h of weak and irregular uterine contractions. She was admitted to the high dependency unit for trial of labour. The haemodynamic variables at various stages of labour are summarized in figure 1. She was managed throughout labour with lateral uterine displacement. Cardiotocography via an abdominal transducer confirmed fetal well-being and maternal cardiovascular monitoring was commenced: ECG monitoring was continued throughout labour and direct arterial pressure monitoring was undertaken via a 20-gauge radial arterial cannula. A pulmonary artery flotation catheter was sited via the right internal jugular vein. A lumbar extradural catheter was sited at the L3–4 interspace and flushed with 0.9 % saline. When uterine contractions became moderately painful, fentanyl 50 μg in 10 ml of 0.9 % saline was injected via the extradural catheter, resulting in significantly attenuated pain and marked reduction in distress, the patient complaining only of mild discomfort with each contraction. She remained haemodynamically stable, sleeping intermittently, until 3 h later, when an oxytocin infusion was started to augment labour; she was observed to become markedly distressed by the increase in frequency and intensity of uterine contractions, requesting additional analgesia. A concomitant sharp increase in pulmonary capillary wedge pressure and a reduction in systemic arterial pressure was observed. Because this haemodynamic deterioration was felt to be caused by increased endogenous adrenergic activity impairing left ventricular ejection, it was decided to commence β adrenergic block therapy and an infusion of esmolol was commenced at 25 μg kg⁻¹ min⁻¹. An additional bolus of fentanyl 50 μg was given via the extradural catheter, again markedly reducing the pain. Within 10 min of administration of additional analgesia and beginning the esmolol infusion, maternal cardiovascular variables stabilized. Fetal heart rate, however, decreased from 140 to 100 beat min⁻¹ with loss of beat-to-beat variability. These cardiotocographic changes persisted throughout the rest of the first stage of labour, which lasted another 30 min.

When the patient expressed a desire to bear down, the uterine cervix was found to be fully dilated. Fetal
of measurements showed a pH of 7.19 and a base excess at 1 and 5 min. Umbilical cord venous blood-gas intervals after delivery and was asymptomatic at 6 months postpartum. She was assessed as an outpatient at third postpartum day, where her recovery was uncomplicated. She was assessed as an outpatient at intervals after delivery and was asymptomatic at 6 months postpartum. After delivery, neonatal Apgar scores were 8 and 9 at 1 and 5 min. Umbilical cord venous blood-gas measurements showed a pH of 7.19 and a base excess of -13.9. Heart rate was 100–120 beat min⁻¹ and mean arterial pressure was 34–39 mm Hg. The infant was admitted to the neonatal intensive care unit for observation where he was noted to be alert but mildly hypotonic and to feed poorly. Blood glucose concentrations were moderately reduced at 2–3 mmol litre⁻¹. Hypotension was treated with 4.5 % human albumin solution and hypoglycaemia corrected with 10 % glucose. Thirty-six hours after delivery all variables were within normal limits. Because of the possibility of HOCM in the neonate, a screening echocardiogram was performed at 2 days which showed a structurally normal heart with good function.

Discussion

Hypertrophic obstructive cardiomyopathy, also termed idiopathic hypertrophic subaortic stenosis, is a disease transmitted by autosomal dominant inheritance, with variable penetrance, characterized by hypertrophy of the cardiac muscle cell [1]. Asymmetrical septal hypertrophy and left ventricular hypertrophy lead to left ventricular outflow tract obstruction with a hypercontractile and poorly compliant left ventricle. Impaired diastolic filling results in raised left ventricular end-diastolic, left atrial and pulmonary artery pressures [2].

Characteristically, echocardiography shows muscular hypertrophy with left atrial enlargement, systolic anterior motion of the anterior mitral valve leaflet and a dynamic gradient between the ventricle and the aorta proportional to the severity of the outflow tract obstruction. Affected patients may be asymptomatic or experience palpitations, angina, syncope and symptoms of left ventricular failure, and are prone to atrial or ventricular rhythm disturbances. HOCM is a recognized cause of sudden death in young people [3].

β Adrenergic block reduces contractility and heart rate, thereby increasing diastolic filling time and improving ventricular filling. Conversely, endogenous or exogenous inotropic agents impair cardiac output by worsening hypercontractility and increasing heart rate.

Although pregnancy is generally well tolerated [4, 5], patients with HOCM usually experience deterioration in symptoms during pregnancy. Indeed, as with out patient, latent disease may become manifest [6]. Sudden death in pregnancy has been reported [7]. The combination of physiological changes and altered haemodynamic state during pregnancy and labour may, in theory, improve or worsen the symptoms of the disease; physiological hypervolaemia increases left ventricular end-diastolic volume and improves cardiac output. Vaso-dilatation, however, may decrease systemic vascular resistance and reduce venous return. Adequate cardiac output is dependent on preload and thus aortocaval compression is tolerated poorly. During labour, the increase in intravascular volume during uterine contractions may improve cardiac output. This is offset by increases in adrenergic activity caused by pain and anxiety. Aortocaval compression, hypovolaemia and the Valsalva manoeuvre during expulsive efforts, may contribute to reductions in venous return, thus impairing cardiac output. Effective analgesia during labour is desirable, both to minimize myocardial sympathetic stimulation and to...
allow assisted delivery to minimize the period of bearing down; extradural and subarachnoid anesthesia should be used with caution because of their potential to reduce preload and afterload [8, 9], and if vasopressors are required, a pure α adrenoceptor agonist such as metaraminol is preferable to vasoconstrictors with inotropic action. Extradural opioids do not cause loss of sympathetic tone associated with local anaesthetic agents and, used alone as in our patient, may be effective. Despite the exaggerated physiological effects of labour in these patients, vaginal delivery is considered safe, provided that factors likely to precipitate haemodynamic disturbances are minimized. Caesarean section is generally reserved for obstetric indications [4].

Continuous invasive haemodynamic monitoring has been used successfully in the management of two parturients with HOCM allowing early detection of increases in pulmonary capillary wedge pressure and assisting in monitoring fluid replacement [10]. It was decided to site a pulmonary artery catheter electively in this patient, because of the severity of the disease and the previous episode of left ventricular failure. The readings permitted titration of the esmolol infusion and, had local anaesthetic agents, with their potentially undesirable side effects in this condition, been necessary for pain relief, would have allowed better monitoring and correction of any resulting haemodynamic disturbances.

Esmolol is a short-acting β adrenoceptor antagonist with no intrinsic sympathomimetic activity [11]. It is administered and titrated easily because of its rapid distribution and elimination half-lives (2 and 9 min, respectively) [12] in non-pregnant patients, and is of particular therapeutic use in situations where rapid onset and short duration of action are required [13]. Its low lipid solubility and rapid metabolism suggest that it may have limited placental transfer, which may confer an advantage over long established beta blocking agents whose use during pregnancy and labour has been limited by concern over fetal effects [14, 15]. Longer acting drugs such as propranolol may be metabolized slowly by the fetus as a result of immature hepatic enzymes, leading to adverse effects, particularly neonatal bradycardia and hypoglycaemia [16]. A study of the effects of short infusions of esmolol in fetal lambs showed rapid, although small, transplacental pass-

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in undelivered pregnant human patients [19, 20] resulted in a decrease in fetal heart rate soon after starting the infusion, with a prompt return to baseline values after its withdrawal. Esmolol used to terminate episodes of tachyarrhythmia in pregnant women at term resulted in features of β block for 48 h into the neonatal period [21] and profound fetal bradycardia necessitating emergency Caesarean section [22].

On the basis of these few investigations and case reports, fetal effects after infusion of esmolol usually appear to be short-lived with no lasting sequelae. We observed persistent hypotonia, hypotension, hypoglycaemia and bradycardia after delivery in the infant of our patient, most likely attributable to the residual effects of the esmolol infusion. These features of β block occurred despite avoidance of an initial loading dose and the low infusion rate administered over a short period. Because the fetal sympathetic system is immature, β block may impair fetal tolerance to hypoxic episodes by abolishing compensatory vasodilatation and the increase in cardiac output which normally increases utero-placental blood flow [23, 24]. This may have contributed to the fetal metabolic acidosis that was observed. The loss of beat-to-beat variation and bradycardia was probably a direct effect of esmolol because of the temporal relationship between the two, but changes in uterine perfusion secondary to maternal cardiac output may have also been partly responsible [17].

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