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Primary Pulmonary Hypertension and Pregnancy: Anesthetic Management for Delivery

FRÉDÉRIQUE SLOMKA, M.D., SERGIO SALMERON, M.D., PAUL ZETLAOUI, M.D., HENRI COHEN, M.D., GÉRALD SIMONNEAU, M.D., KAMRAN SAMII, M.D.

Young women in childbearing age represent almost 80% of the patients suffering from primary pulmonary hypertension (PPH). They are at serious risk of deterioration during pregnancy, labor, and puerperium, leading to maternal death.[1] Thus, patients with PPH are advised to avoid pregnancy and to consider termination of pregnancy if it occurs. In some cases the patients wish to become pregnant and refuse therapeutic abortion. We report the management of such a case.

CASE REPORT

In a 32-yr-old nulliparous woman presenting with dyspnea increasing for one year, PPH was diagnosed and hemodynamically investigated; three vasodilators isoproterenol, prostacyclin, and diltiazem were tested intravenously (table 1). All three were found to have a marked vasodilator effect characterized by a 50% decrease of pulmonary vascular resistance (PVR), together with a reduction in pulmonary arterial pressure (PAP) and an increase in cardiac output. Therapy then began with oral diltiazem 180 mg daily. Three months later she became pregnant. Diltiazem was then discontinued because the fetal effects of diltiazem are unknown. She was then treated with oral isoproterenol 50 mg daily, without any increase in dyspnea or antenatal complication.

It was planned to induce labor at 38 weeks gestation. The day before induction of labor baseline hemodynamic values were recorded after pulmonary artery catheterization *via* the internal jugular vein. Baseline measurements showed no worsening of the disease during pregnancy (table 1). The effects of left uterine displacement and isoproterenol, oxytocin, and ephedrine administration (table 1) were then studied, anticipating use of these drugs during management of labor. Isoproterenol (0.2 mg/h) reduced PAP and PVR. Oxytocin (5 mU/min) did not change these variables, whereas ephedrine increased PAP and cardiac output with no change of PVR.

A double catheter epidural analgesia technique was used. The upper catheter, used to block the thoracolumbar segments during the first stage of labor, was placed at L1-2 level and directed cephalad. The second catheter was placed at the L4-5 level and directed caudally for the perineal predelivery anesthesia. There were no appreciable hemodynamic changes following injection of 10 ml of bupivacaine 0.25% through the upper catheter, with good pain relief and a sensory dermatome level extending from T_7 to L_1. Bupivacaine 0.25% was used throughout labor and delivery. Heparin infusion (200 IU $\cdot$ kg^{-1} $\cdot$ 24 h^{-1}) was started[2] one hour after the epidural catheters were inserted.[3] A mild left lateral position was used to avoid aortocaval compression. Oxytocin augmentation of labor was started after artificial rupture of membranes.

Because uterine contractions were associated with increases in PAP and PVR, isoproterenol infusion was started at a rate of 0.2 mg/h, resulting in a decrease in PVR but leading to a severe systemic hypotension with tachycardia for which 500 ml of colloids were infused with restoration of a normal systemic arterial pressure without reduction in the tachycardia and a reduced frequency of uterine contractions. Thus, isoproterenol was stopped, and labor continued for 8 hours without hemodynamic complication.

A predelivery dose of 15 ml of 0.25% bupivacaine was injected in two increments through the lower catheter resulting in perineal anesthesia adequate for forceps vaginal delivery of a 3800 g male infant. Apgar scores were 10 at both one and five minutes. One hour after delivery a 20% increase in PVR led us to restart the isoprenaline infusion (0.2 mg/h), which was effective and well tolerated (table 1). There was no sign of right ventricular failure and the patient was discharged from the intensive care unit two days later while being given oral isoproterenol 50 mg daily and heparin. To determine if amniotic fluid embolism might have occurred, blood samples were withdrawn from the pulmonary arterial catheter during the seventh hour of labor and after delivery. No fetal cells were found. Three weeks after delivery when breast-feeding had stopped, diltiazem 180 mg daily was reintroduced. Twelve months after delivery right heart catheterization showed no worsening of the pulmonary hypertension.

DISCUSSION

PPH is often exacerbated by pregnancy. Especially dangerous is development of heart failure, the risk of which is greatest during the third trimester and in the peripartum period when the mortality rate reaches 50%.[1] Moreover, because pulmonary vascular reactivity to drugs is usually reduced during pregnancy,[2,4] therapy may be less than fully effective.

The anesthetic management of patients with PPH during delivery is poorly documented. Several principles have been suggested by Mangano.[5] The first principle is that the degree of pulmonary hypertension and right ventricular failure must be assessed before proceeding with anesthesia. The reactivity of the pulmonary vasculature should also be studied to determine if pharmacologic pulmonary vasodilation is feasible.[5] In our case all drugs tested before pregnancy (prostacyclin, diltiazem, and isoproterenol) produced a marked decrease in PVR, which is not the most common response.[6] Diltiazem was chosen for long-term oral treatment because oral prostacyclin is not available and oral isoproterenol has a short duration of action requiring many daily intakes. However, after confirmation of pregnancy oral isoproterenol was given

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Address reprint requests to Dr. Samii: Département d'Anesthésiologie, Hôpital Antoine Béclère, 157 rue de la Porte de Trivaux, 92140 Clamart, France.

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TABLE 1.

	Baseline	ISO* (0.4 mg/h)	PGI_2* (10 ng/kg/h)	Diltiazem* (20 mg/h)	Supine	LUD	Supine ISO (2.0 mg/h)	Supine Oxytocin† (5 mU/min)	Supine Ephedrine† (5 mg)	Baseline	ISO (0.2 mg/h)	Diltiazem (20 mg/h)
RAP (mmHg)	0	0	0	0	2	7	0	3	3	5	4	5
PAP (mmHg)												
Systolic	80	43	44	51	72	80	33	69	92	86	56	57
Mean	48	26	27	27	48	52	25	45	63	55	36	38
Diastolic	36	22	22	15	37	30	19	35	44	37	24	24
MPWP (mmHg)	1	0	4	3	7	6	1	5	8	4	7	4
MAP (mmHg)	95	95	93	97	85	93	72	93	107	96	80	96
CI ($l \cdot min^{-1} \cdot m^{-2}$)	3.2	5.4	4.1	4	3.6	4	4	3.8	5.1	3.8	4.5	4.3
HR (beats/min)	70	80	80	70	80	74	138	80	70	80	130	90
PVR ($mmHg \cdot l^{-1} \cdot min^{-1} \cdot m^{-2}$)	14	4.8	5.6	6.5	11.4	11.5	6	10.5	10.8	13.4	6.4	7.9
SVR ($mmHg \cdot l^{-1} \cdot min^{-1} \cdot m^{-2}$)	29	17.5	22	24	23	21.5	18	23.6	20.8	24	16.8	21

ISO = isoproterenol; PGI_2 = prostacyclin; LUD = left uterine displacement; RAP = right atrial pressure; PAP = pulmonary artery pressure; MPWP = mean pulmonary wedge pressure; MAP = mean arterial pressure; CI = cardiac index; HR = heart rate; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance.

* Time interval between ISO, PGI_2, and diltiazem was 15 min.

† Time interval between oxytocin and ephedrine was one hour.

throughout pregnancy to avoid any possible deleterious fetal effect of diltiazem. The maintained beneficial clinical effect of isoproterenol was confirmed on the day before delivery by the important reduction of PVR (table 1).

The second principle is that the management of delivery has the primary goal of minimizing increases in PVR related to hypercarbia, hypoxia, acidosis, stress, and pain.[5] For this reason the method of delivery should be discussed with the patient and the obstetrician because anesthesia may have a deleterious impact on the hemodynamic status. Cesarean section was not mandatory for obstetric reasons (vaginal delivery is usually accepted when the following criteria are met: singleton fetus in cephalic presentation with normal cardiotocogram, absence of cephalopelvic disproportion and of placenta previa). Moreover, regional anesthesia for cesarean section may produce a large decrease in venous return because the upper level of the block needs to be extended up to T_4, with a large sympathetic block.[7] However, general anesthesia may increase pulmonary artery pressure during laryngoscopy,[8] and some authors have thus suggested a progressive inhalation induction with halothane to reduce PVR, although a potential risk for aspiration exists.[5] In our patient vaginal delivery was chosen and labor was successfully induced with oxytocin after confirmation of the absence of hemodynamic effects of usual doses. To avoid increases in PVR, we reduced pain and stress with epidural anesthesia. Intrathecal morphine for relief of labor pain in a patient with pulmonary hypertension has been previously reported to produce effective analgesia without any decrease in cardiac output.[9] In this report,[9] however, the patient was para 5 and pain may have been more moderate than in our patient who was primipara and in whom labor was managed with oxytocin. Vaginal delivery with segmental epidural analgesia with local anesthetics has been previously reported,[10] but it was associated with a pudendal block to provide perineal analgesia for delivery. Recently, Robinson and Leicht reported the management of labor and delivery using analgesia with low-dose bupivacaine and fentanyl in a parturient with severe PPH.[11] In our patient the use of two epidural catheters followed the same principle of segmental analgesia with local anesthetics, and a systematic instrumental extraction was performed to avoid Valsalva maneuvers during expulsive efforts.

The third principle is that major hemodynamic changes should be avoided including decreases in systemic vascular resistance and drug-induced myocardial depression.[5] More importantly, marked decreases in venous return caused by lung inflation, aortocaval compression, or by a major conduction anesthesia must be minimized.[6] To avoid large changes in the loading conditions of the right ventricle and in systemic vascular resistances, epidural analgesia was performed with relatively small increments of 0.25% bupivacaine. Meticulous attention was given to changes in venous return by continuous infusion of fluids.

Ephedrine was tested and did not change the PVR. However, hemodynamic measurements showed increases in PAP and CI associated with contractions, together with increases in PVR. Uterine contractions are known to diminish the volume of blood retained in the dilated uterine veins[12]; thus, blood is expelled into the systemic circulation producing autotransfusion and increases in cardiac output and PAP. We have no pathophysiologic explanation for the increase in PVR because the patient was pain-free and did not exhibit any sign of hypercarbia, hypoxemia, or acidosis. Nevertheless, the infusion of isoproterenol, which was started to reduce these peaks of PVR during contractions, was associated with hypotension and tachycar-

dia, resulting likely from the potentiation of the vasodilation of epidural analgesia. The isoproterenol-induced decrease in frequency of uterine contractions was related to its beta adrenergic effect because the rate of the isoprenaline infusion (0.2 mg/h) was in the range of what is known to reduce uterine contractions.[13]

The postpartum period is critical in women with PPH because dramatic increases in PVR generally precede irreversible right ventricular failure and death.[14] The increase in PVR appears usually unresponsive to vasodilator drugs, but rarely, as in the present report, vasodilator drugs may be efficient.[1] The mechanism involved in the increase in PVR remains unknown. It has been suggested that amniotic fluid embolism might be a worsening factor in PPH.[2] However, histologic examination in patients who had been pregnant showed no features that could be interpreted as residue of amniotic embolism.[2] In our patient blood samples were withdrawn from the pulmonary artery and did not show any evidence of amniotic fluid embolism. However, it has been suggested that widespread thrombosis of the small vessels in the pulmonary arterial system occurs in the postpartum period, further aggravating pulmonary hypertension.[2] For this reason prophylactic heparin infusion was started one hour after epidural catheterization, according to Rao and El-Etr who have shown that such a technique is associated with very rare and self-limited neurologic complications.[3]

In conclusion, when pregnancy cannot be avoided or terminated early in patients with PPH, vasodilator treatment is difficult because drugs are either contraindicated or of poor efficacy.[15] In the present case isoproterenol fortunately remained efficient to reduce PVR before, during, and after pregnancy. Management of labor should include methods to avoid causes of increases of PVR and decreases of right ventricular preload. Lumbar segmental epidural analgesia is especially useful in this context, but small increments of low concentrations of local anesthetics should be used to maintain right ventricular function. Hemodynamic monitoring is mandatory.

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