The Effect of Phenoxybenzamine on the Pulmonary Vascular Bed in Surgically Corrected Ventricular Septal Defect Associated with Pulmonary Hypertension

Kyoichi OGAWA, M.D., Tetsuo YAMAMOTO, M.D., Sakae ASADA, M.D.,
Seizo IWAI, M.D., Akira TORIYAMA, M.D., Kazuhiko HORIKOSHI, M.D.,
Masahiro YAMAGUCHI, M.D., and Ken KIMURA, M.D.

SUMMARY

From 1971 to 1977, a total of 43 cases with ventricular septal defect associated with pulmonary hypertension (VSD+PH), ranging from 3 months to 6 years of age, underwent VSD closure using cardiopulmonary bypass with a prophylactic dose of phenoxybenzamine (POB) 1 mg/Kg. Twenty of these cases are included in the present study of the effect of POB on pulmonary hypertension. The ratios of pulmonary to systemic arterial pressures (Pp/Ps) and vascular resistances (Rp/Rs) were measured before, immediately after and 1 month after VSD closure. In all cases, the Pp/Ps before VSD closure was larger than 0.75. Both Pp/Ps and Rp/Rs markedly decreased immediately after VSD closure but rose again 1 month thereafter. These results suggest the possibility of pulmonary vasodilating effect of POB, which could be potentially useful in relieving the right ventricular load in the early postoperative period. The over all mortality was 3 out of 43 cases including 2 late deaths.

Additional Indexing Words:

Cardiopulmonary bypass Pulmonary vascular resistance Ratio of pulmonary to systemic arterial pressures (Pp/Ps) Ratio of pulmonary to systemic vascular resistances (Rp/Rs) Correction of ventricular septal defect Low cardiac output syndrome

PHENOXYBENZAMINE(POB) is a specific alpha-receptor blocking agent which reduces peripheral vascular resistance, permitting an increase in cardiac output.¹⁾ In cardiac surgery, this agent has been used to improve hypoperfusion states during and after cardiopulmonary bypass.²⁾⁻⁶⁾ Recent report has commented upon a selective pulmonary vasodilating effect of POB, which was demonstrated in a preoperative cardiac catheterization.³⁾ This

From the Second Surgical Department, the Department of Anesthesiology, Kobe University School of Medicine and the Department of Surgery, Kobe Children's Hospital.

Address for reprints: Kyoichi Ogawa, M.D., Second Surgical Department, Kobe University School of Medicine, Kusunoki-cho 7, Ikuta-ku, Kobe 650, Japan.

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report agrees with our results of POB during corrective surgery for ventricular septal defect (VSD) associated with pulmonary hypertension (PH), specifically to reduce pulmonary vascular resistance in order to relieve the right ventricular load during the immediate postoperative period.

From 1971 to 1977, 43 VSD+PH cases from 3 months to 6 years of age underwent VSD closure using cardiopulmonary bypass with a prophylactic dose of POB (1 mg/Kg). In all cases, the ratio of pulmonary to systemic arterial pressures (Pp/Ps) was larger than 0.75, preoperatively. In the most recent 20 consecutive cases, pulmonary and systemic arterial pressures were recorded before, immediately after and 1 month after operation. The Pp/Ps and the ratio of pulmonary to systemic arterial resistances (Rp/Rs) were calculated for the study of the effect of POB on the pulmonary vascular resistance. This paper will present and discuss the effect of POB on pulmonary vascular resistance in VSD+PH.

MATERIALS AND METHODS

Of the 43 cases of VSD+PH undergoing corrective surgery with POB, 20 cases were subjected to the present study. For bypass procedure, a Temptrol bubble oxygenator was primed with lactate Ringer solution and heparinized blood providing 30% hemodilution of total circulating blood volume. An aortic cannula was connected to the arterial line of the oxygenator with a pump-output of 2.4 to 3.2 L/M²/min under normothermia or mild hypothermia (28–36°C). After aortic cannulation, an infusion of POB (1 mg/Kg, diluted in 30 to 50 ml of 5% dextrose in water) was started 15 to 30 min prior to the beginning of bypass. During administration of POB, blood was transfused to correct the relative hypovolemia resulting from POB administration, which was monitored by blood pressure and central venous pressure. Cardiopulmonary bypass was started at the completion of POB administration. At the end of the intracardiac procedures, systemic and pulmonary arterial pressures were simultaneously recorded, while the patients inspired 50% oxygen. One month after operation, all cases underwent cardiac catheterization under general anesthesia with inspiration of 50% oxygen, and the Pp/Ps and Rp/Rs were calculated.

RESULTS

The Pp/Ps before operation ranged from 0.75 to 1.16 with a mean of 0.94. At the end of intracardiac procedures, the Pp/Ps became 0.20 to 0.66 with a mean of 0.41. One month after operation, the Pp/Ps rose to the range of 0.25 to 1.02 with a mean of 0.56 (Fig. 1).

The preoperative Rp/Rs ranged from 0.08 to 0.87 with a mean of 0.48. At the end of correction of VSD, the value ranged from 0.16 to 0.50 with a

Fig. 1. The ratio of pulmonary to systemic arterial pressures before, immediately after correction of VSD and 1 month after operation.

Fig. 2. The ratio of pulmonary to systemic arterial resistances before, immediately after correction of VSD and 1 month after operation.

mean of 0.34. One month after operation, the R_p/R_s ranged from 0.21 to 0.91 with a mean of 0.49 (Fig. 2).

In 4 of the 20 cases, the R_p/R_s measured 1 month after operation was more than 0.70. However, the R_p/R_s at the end of intracardiac procedures was below 0.42 in all 4 cases. Of a total of 43 cases undergoing correction of VSD with POB, 1 operative death was encountered. The patient died of ventricular arrhythmia on the 10th postoperative day, the cause of which was unknown. The 2 other cases died of respiratory failure on the 110th and

162nd postoperative days respectively. No mortality occurred in the most recent 20 cases which were subjected to this study.

DISCUSSION

After correction of VSD, remaining high pulmonary vascular resistance is one of the most serious problems affecting operative results as pointed out by Cartmill et al,⁷⁾ and others.^{8),9)} Persistent high pulmonary vascular resistance after closure of VSD increases right ventricular load during the immediate postoperative period, resulting in low cardiac output state and in increased mortality.

The acute fall of Pp/Ps and Rp/Rs seen immediately after correction of VSD is assumed to be the results of both anatomical closure VSD and the effect of POB to dilate the pulmonary vascular bed. Because the rise of Pp/Ps and Rp/Rs 1 month after the operation was seen in a total of 16 cases among the 20, POB is assumed to be significantly effective in reducing pulmonary vascular resistance.

Other factors reducing pulmonary vascular resistance, such as tolazoline hydrochloride (priscoline),¹⁰⁾ hexamethonium bromide (C₆),¹¹⁾ acetylcholine,¹²⁾ oxygen,^{13),14)} and artificial ventilation¹⁵⁾ etc have also been reported.

Because artificial ventilation using high concentration of oxygen is routinely used during the immediate postoperative period, the effect of these factors is not negligible. Therefore, we measured pulmonary and systemic pressures under general anesthesia with 50% oxygen inspiration preoperatively, during operation and postoperatively, to eliminate the effect of above mentioned factors.

As for the effect of POB on pulmonary vascular resistance, Ohta et al,³⁾ reported that a decrease of Pp/Ps from 0.80 to 0.71 and Rp/Rs from 0.59 to 0.40 were observed after the administration of POB in cases of patent ductus arteriosus associated with pulmonary hypertension (PDA+PH) and VSD+PH during preoperative cardiac catheterization. To our knowledge, no report has ever been presented about the effect of POB on pulmonary vascular resistance concerning the corrective surgery of VSD+PH.

Many authors including us have already reported that POB markedly reduces systemic vascular resistance in clinical subjects.¹⁾⁻⁶⁾ In this series of 43 surgical cases of VSD+PH including twelve infants under 12 months of age, only 1 operative death was seen in a 3-month-old baby who developed ventricular arrhythmia on the 10th postoperative day. Low cardiac output syndrome was noticed in only 2 cases including the dead case.

According to the results, it may be concluded that the effect of POB

in reducing both systemic and pulmonary vascular resistances seemed to prevent low cardiac output syndrome by decreasing cardiac load and resulted in satisfactory outcomes in this series.

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