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Verapamil reduced pulmonary hypertension in adult respiratory distress syndrome

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Introduction

Pulmonary hypertension is usually seen in adult respiratory distress syndrome (ARDS), which causes an acute increase in the work load on the right ventricle [1]. The management of pulmonary vascular resistance (PVR) is beneficial to right ventricular function because the PVR in survivors of ARDS tends to decrease during therapy [2]. In the present paper, we describe a patient in whom verapamil reduced PVR more effectively than prostaglandin E_1 (PGE_1).

Case report

A 24-year-old man was admitted for posttraumatic respiratory failure. He broke his right femur in a traffic accident and developed dyspnea 30 h after the accident. His hemoglobin concentration was maintained above 9.9 $g \cdot dl^{-1}$ by transfusion of 1000 ml of whole blood. Hypovolemic shock was not associated with the onset of respiratory failure. A chest X-ray showed bilateral ill-defined parenchymal infiltrates. Arterial blood gas analysis showed a pH of 7.42, Pao_2 of 56 mmHg, $Paco_2$ of 47 mmHg under mechanical ventilation with an inspired oxygen fraction (FIO_2) of 1.0 and a positive end expiratory pressure (PEEP) of 10 cmH_2O. A flow-directed pulmonary artery (PA) catheter was inserted via the right internal jugular vein into the pulmonary artery to evaluate hemodynamics (Table 1). Forty-five h after the fracture (on the 3rd hospital day), the mean pulmonary arterial pressue (mPAP) was 29 mmHg and pulmonary vascular resistance index (PVRI) showed 397 $dyn \cdot sec \cdot cm^{-5} \cdot m^{-2}$. On the 4th hospital day, the PA catheter was withdrawn 72 h after insertion, although no remarkable change was seen in PAP. Pao_2/FIO_2 remained 100–150 with an FIO_2 of 0.6–0.8 and 10 cmH_2O PEEP without any radiological improvement. On the 7th hospital day, PGE_1 and dopamine were administered at 30 $ng \cdot kg^{-1} \cdot min^{-1}$ and 3–5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, respectively, and the PEEP was increased to 20cmH_2O. During the next 4 days, no improvement was seen in arterial oxygen tension. The heart rate was 120–150 $b \cdot min^{-1}$ with a normal sinus rhythm. On the 13th hospital day (6 days after the start of PGE_1 infusion) a PA catheter was reinserted via the right internal jugular vein to evaluate the effects of PGE_1 on hemodynamics under the 20cmH_2O PEEP (Table 1). Because the PVRI showed no improvement compared with the values on the 3rd hospital day, PGE_1 was discontinued and verapamil was administered at a rate of 2.5 $mg \cdot h^{-1}$ to control tachycardia and pulmonary hypertension. One h after the start of the infusion of verapamil, heart rate decreased from 124 min^{-1} to 114 min^{-1}, cardiac index increased from 3.54 $L \cdot min^{-1}$ to 4.89 $L \cdot min^{-1}$, PVRI decreased from 384 $dyn \cdot sec \cdot cm^{-5} \cdot m^{-2}$ to 262 $dyn \cdot sec \cdot cm^{-5} \cdot m^{-2}$, and central venous pressure (CVP) decreased from 18 mmHg to 14 mmHg, although the mean arterial pressure and mPAP remained unchanged. During the next 2 days (on the 14th and 15th hospital day), PVRI further decreased to 181 $dyn \cdot sec \cdot cm^{-5} \cdot m^{-2}$, mPAP decreased gradually from 36 mmHg to 27 mmHg, heart rate decreased to 93 min^{-1}, cardiac output increased to 10.0 $L \cdot min^{-1}$, and Pao_2/FIO_2 increased to 230. Dopamine was discontinued on the 16th hospital day and verapamil was tapered and discontinued on the 22nd hospital day. He was weaned gradually from the ventilator from the 22nd hospital day and extubated on the 31st hospital day.

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Table 1. Effects of verapamil on hemodynamics and oxygenation index

	Onset	13th day PGE_1 30 ng·kg^{-1}·min^{-1}	1 h	24 h	48 h
			after start of verapamil 2.5 mg/h (without PGE_1)		
HR (b·min^{-1})	99	124	114	101	93
MAP (mmHg)	76	98	100	90	88
mPAP (mmHg)	29	36	37	31	27
RAP (mmHg)	7	18	14	17	13
PCWP (mmHg)	11	19	21	20	15
C.I. (L·min·m^{-2})	3.62	3.54	4.89	4.12	5.30
SVRI (dyn·sec·cm^{-5}·m^{-2})	1660	1808	1407	1417	1132
PVRI (dyn·sec·cm^{-5}·m^{-2})	397	384	262	213	181
LVSWI (gram-meters·m^{-2})	32.3	30.7	46.1	38.8	56.6
RVSWI (gram-meters·m^{-2})	10.9	7.0	13.4	7.8	10.9
Pao_2/FIO_2	198	137	118	120	230

HR, heart rate; mAP, mean arterial pressure; mPAP, mean pulmonary arterial pressure; RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; C.I., cardiac index; SVRI, systemic vascular resistance index; PVRI, pulmonary vascular resistance index; LVSWI, left ventricular stroke work index; RVSWI, right ventricular stroke work index; Pao_2/FIO_2, oxygenation index.

Discussion

The pathogenesis of ARDS is still controversial and its treatment is supportive [3]. There are several causes of pulmonary hypertension in ARDS: acute pulmonary vasoconstriction, increased interstitial pressure, microembolism or thrombosis, endothelial cell edema, microvascular obliteration by fibrosis, or extravascular hemorrhage [1]. We cannot distinguish with certainty which of these pathological changes were improved by verapamil. Verapamil is a well-known vasodilator with a calcium channel blocking effect. We speculated that verapamil produced pulmonary vasodilatation, because verapamil can prevent hypoxic pulmonary vasoconstriction in an experimental model [4]. Another possibility is the inhibition of eicosanoides. Verapamil attenuates the endotoxin-induced increase in pulmonary vascular resistance and endotoxin-induced changes in thromboxane B2 and 6-ketoprostaglandin $F_{1\alpha}$ [5]. PVR is reduced by direct pulmonary vasodilation or and recruitment of vasculature. An appropriate increase in cardiac output is necessary to maintain total oxygen delivery during ARDS [6]. Although verapamil reduced right ventricular afterload through pulmonary vasodilation, it might directly depress right ventricular function [7]. Right ventricular performance, as reflected by right ventricular stroke work index, did not deteriorate with verapamil in this case. Since stroke volume increased and PVR decreased, the increase in right ventricular stroke work index was not due to the increase in pressure work but due to the increase in volume work. Because pulmonary vascular resistance was not improved by infusion of PGE_1, we stopped PGE_1 and replaced it with verapamil. In general, the beneficial effect of PGE_1 on the pulmonary circulation in ARDS is to reduce pulmonary arterial pressure and pulmonary vascular resistance [2,6]. Verapamil, however, produced a more beneficial effect on mPAP, PVR, heart rate, and cardiac output than PGE_1 in this case. PGE_1 is also known to increase heart rate and induce dysrhythmias including supraventricular tachycardia and rapid atrial dysrhythmias in ARDS [8]. In summary, we used verapamil to reduce right ventricular afterload and found that verapamil may be an effective pharmacologic agent for the reduction of PAP in ARDS.

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