Phenylephrine increases pulmonary blood flow in children with tetralogy of Fallot

[La phényléphrine augmente le débit sanguin chez les enfants qui présentent une tétralogie de Fallot]

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Purpose: Although it has been reported that the increase in blood pressure improves arterial oxygen saturation (SaO_2) in children with tetralogy of Fallot, no prospective study has demonstrated that an increase in blood pressure induces an increase in pulmonary blood flow in these patients. The purpose of this study was to see whether a phenylephrine-induced increase in systemic blood pressure increased pulmonary blood flow, resulting in improved arterial oxygenation in tetralogy of Fallot.

Methods: In 14 consecutive children with tetralogy of Fallot (2–32 months old), transesophageal pulsed Doppler signals of left upper pulmonary venous flow (PVF) velocity were recorded before and four minutes after 10 $\mu g \cdot kg^{-1}$ of phenylephrine *iv*. Simultaneously, arterial blood gas analysis and hemodynamic measurements were performed. The minute distance (MD) was calculated as the product of the heart rate and the sum of time-velocity integrals of PVF.

Results: Phenylephrine *iv* increased mean arterial blood pressure from 54 ± 8 mmHg to 73 ± 10 mmHg. This phenylephrine-induced hypertension significantly increased SaO_2 and MD (92.0 ± 7.5 *vs* 95.0 ± 5.0% and 1318 ± 344 *vs* 1533 ± 425 $cm \cdot min^{-1}$, respectively). There was a significant correlation ($r = 0.72$) between the change in MD and the change in SaO_2.

Conclusion: Our results suggest that the phenylephrine-induced increase in systemic blood pressure produces an increase in pulmonary blood flow in tetralogy of Fallot. Our results further suggest that this increase in pulmonary blood flow is involved in the mechanism of phenylephrine-induced improvement of arterial oxygenation in tetralogy of Fallot.

Objectif : *On a déjà montré qu'une augmentation de la tension artérielle améliore la saturation en oxygène du sang artériel (SaO_2), chez les enfants qui présentent une tétralogie de Fallot, mais aucune étude prospective n'a démontré qu'une augmentation de la tension artérielle pouvait induire une élévation du débit sanguin pulmonaire chez ces patients. Nous voulions vérifier si une augmentation de la tension artérielle générale induite par la phényléphrine fait augmenter le débit sanguin pulmonaire et améliore l'oxygénation artérielle dans le contexte d'une tétralogie de Fallot.*

Méthode : *Chez 14 enfants porteurs d'une tétralogie de Fallot et traités consécutivement (âgés de 2–32 mois), les signaux Doppler pulsés transœsophagiens de la vitesse du flux de la veine pulmonaire gauche supérieure (DVP) ont été enregistrés avant, puis quatre minutes après l'administration iv de 10 $\mu g \cdot kg^{-1}$ de phényléphrine. Une analyse des gaz du sang artériel et des mesures hémodynamiques ont été réalisées simultanément. La distance minute (DM) a été calculée comme le produit de la fréquence cardiaque et de la somme des intégrales de temps-vélocité du DVP.*

Résultats : *La phényléphrine iv a augmenté la tension artérielle moyenne de 54 ± 8 mmHg à 73 ± 10 mmHg. L'hypertension induite par la phényléphrine a augmenté la SaO_2 et la DM de façon significative (92,0 ±7,5 vs 95,0 ± 5,0 % et 1318 ± 344 vs1533 ± 425 $cm \cdot min^{-1}$, respectivement). Il y avait une corrélation significative ($r = 0,72$) entre les modifications de la DM et celles de la SaO_2.*

Conclusion : *Nos résultats suggèrent que, chez les patients atteints d'une tétralogie de Fallot, l'augmentation du débit sanguin général induite par la phényléphrine produit une élévation du débit sanguin pulmonaire. De plus, il apparaît que cette augmentation du débit sanguin pulmonaire contribue à l'amélioration de l'oxygénation artérielle induite par la phényléphrine.*

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AN increase in systemic blood pressure has been reported to improve arterial oxygenation and recovery from anoxic spells in tetralogy of Fallot.[1–5] We previously reported a significant correlation between mean arterial blood pressure and arterial oxygen tension (PaO_2) in patients undergoing complete surgical correction of tetralogy of Fallot.[1] However, there is no evidence indicating that the increase in systemic blood pressure increases pulmonary blood flow (PBF) in these children.

It is critical for anesthesiologists to minimize the difference between systemic blood flow and PBF during operation in children with congenital heart disease. However, measurements of PBF in children with tetralogy of Fallot are clinically limited. The reasons are as follows: 1) placement of the pulmonary artery catheter is limited in small children; 2) measurement of the pulmonary artery flow velocity with pulsed Doppler echocardiography is difficult because of the very high flow velocity produced by pulmonary stenosis; and 3) the blood flow from the collateral vessels or previous anastomosis cannot be measured from the pulmonary artery approach. In contrast, it is relatively easy to obtain pulsed Doppler signals of pulmonary venous flow (PVF) velocity by using transesophageal echocardiography (TEE) even in children with tetralogy of Fallot. Thus, we measured the PVF velocity in the left upper pulmonary vein as an indicator of PBF. The purpose of the current study was to evaluate the effects of phenylephrine-induced hypertension on both PBF and arterial oxygenation.

Methods

The study was approved by the Ethics Committee on Human Study of our hospital. Written informed consent was obtained from the parents of all children enrolled. Fourteen patients undergoing complete surgical correction of tetralogy of Fallot were studied. Eleven of the 14 patients were given ß-blockers preoperatively. Patients were premedicated with atropine or scopolamine, supplemented with *im* hydroxyzine, if necessary, 30 min before induction of anesthesia. Anesthesia was induced and maintained with sevoflurane, oxygen, nitrous oxide, and fentanyl. After tracheal intubation, catheters were placed in the superior vena cava through the right internal jugular vein and in the radial artery, and a 5.0-MHz single-plane TEE probe (UST-5234S-5 or UST-5240S-5; Aloka Co., Ltd., Tokyo, Japan) was inserted orally. Guided by Doppler colour-flow imaging, the TEE probe was positioned to view the left upper pulmonary vein. During the study period, patients were ventilated with 100% oxygen. Before the skin incision, phenylephrine 10 $\mu g \cdot kg^{-1}$ was administered intravenously. PVF velocity was recorded by positioning the Doppler sample volume in the left upper pulmonary vein before (baseline) and four minutes after phenylephrine. Simultaneously, hemodynamic variables and arterial blood gases were measured.

Echocardiographic analysis

PVF tracings were digitized off-line using the SSD-830 (Aloka Co., Ltd., Tokyo, Japan) analysis package. From PVF velocity tracings, we measured peak velocities and time-velocity integrals of the systolic (peak S, TVI-S), early diastolic (peak D, TVI-D), and reversal

TABLE I Patient demographics

Patient no.	*M/F*	*Age (months)*	*Height (cm)*	*Weight (kg)*	*History of palliative shunt*	*Site of pulmonary artery stenosis*	*Other lesion*
1	M	24	85.6	10.6	Lt. Blalock-Taussig	supravalvular	ASD
2	M	16	83.5	11.8	-	infundibular, valvular, supravalvular	-
3	F	25	81.0	11.5	-	supravalvular	-
4	M	32	85.0	10.5	-	infundibular	-
5	F	25	81.0	11.0	-	infundibular, supravalvular	-
6	F	27	87.5	13.0	-	infundibular, valvular	ASD
7	F	10	66.5	5.9	Central shunt	pulmonary atresia	-
8	F	26	82.6	10.8	Lt. Blalock-Taussig	pulmonary atresia	-
9	M	3	63.0	5.7	Rt. Blalock-Taussig	pulmonary atresia	PDA
10	F	2	51.1	4.2	-	pulmonary atresia	PDA
11	F	12	70.8	8.9	-	infundibular, valvular	ASD
12	M	11	71.6	7.2	Lt. Blalock-Taussig	infundibular	-
13	F	10	73.6	8.3	Rt. Blalock-Taussig	pulmonary atresia	-
14	M	25	83.0	12.0	-	valvular	-

M/F = male/female; ASD = atrial septal defect; PDA = patent ductus arteriosus.

TABLE II Hemodynamic variables, arterial blood gas, and Doppler echocardiographic variables recorded before (baseline) and after phenylephrine in children with tetralogy of Fallot

	Baseline	*Phenylephrine*
Hemodynamics variables (n = 14)		
Heart rate (beats·min^{-1})	112 ± 18	97 ± 18*
Systolic arterial pressure (mmHg)	74 ± 12	104 ± 9*
Diastolic arterial pressure (mmHg)	41 ± 7	55 ± 11*
Mean arterial pressure (mmHg)	54 ± 8	73 ± 10*
CVP (mmHg)	7 ± 3	10 ± 3*
Arterial blood gases (n = 14)		
pH	7.37 ± 0.05	7.37 ± 0.05
PaO_2 (mmHg)	109 ± 103	150 ± 138*
$PaCO_2$ (mmHg)	35 ± 4	36 ± 5
Base excess	-4.3 ± 2.7	-4.2 ± 2.3
SaO_2 (%)	92.0 ± 7.5	95.0 ± 5.4*
Pulmonary venous flow velocity integrals (n = 12)		
TVI-S (cm)	6.1 ± 2.2	7.7 ± 2.6*
TVI-D (cm)	5.5 ± 2.2	8.1 ± 3.2*
TVI-R (cm)	0.2 ± 0.6	0.2 ± 0.6
TTVI (cm)	11.4 ± 3.3	15.5 ± 4.9*
Minute distance (cm·min^{-1})	1318 ± 344	1533 ± 425*

Values are mean ± SD. CVP = mean central venous pressure; TVI-S = time-velocity integral of S wave; TVI-D = time-velocity integral of D wave; TVI-R = time-velocity integral of reversal wave; TTVI = total time-velocity integral; TTVI = TVI-S + TVI-D - TVI-R; Minute Distance = TTVI-HR. *$P < 0.05$ *vs* baseline.

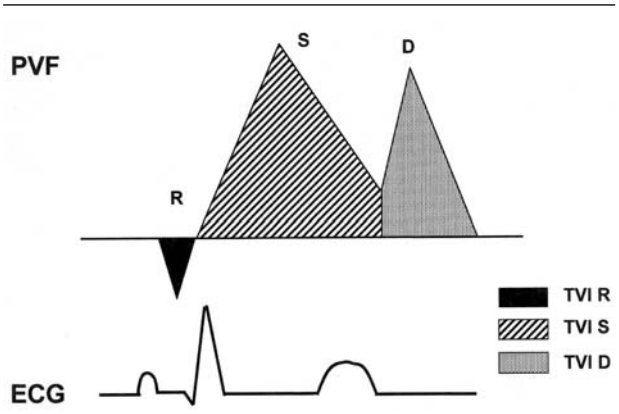

FIGURE 1 Graphic illustration of the normal polyphasic pulmonary venous flow pattern and its relative timing in the cardiac cycle. Normal pulmonary venous flow is composed of systolic (S wave) and diastolic (D wave) forward flow with a small component of reverse flow (R wave). Schematics show measurements of time-velocity integrals (TVI).

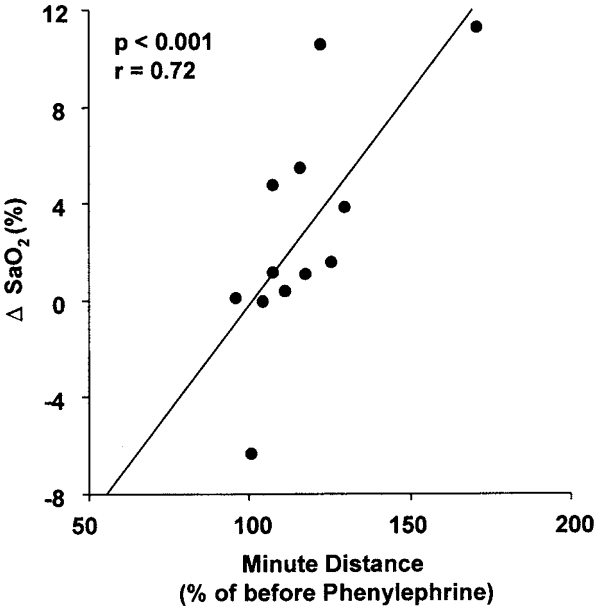

FIGURE 2 Relationship between the changes in minute distance (% before phenylephrine) and the changes in SaO_2 (Δ SaO_2; the difference between before and after phenylephrine) in 12 children with tetralogy of Fallot.

(peak R, TVI-R) waves (Figure 1).[6] Three consecutive beats were traced, and the results were averaged in each patient. The minute distance (MD) of the left upper pulmonary vein was defined as the product of total time-velocity integrals (TTVI, TVI of S + D - R waves) and heart rate.

Statistical methods

Values were expressed as mean ± SD. The correlation between percent changes in the MD (Δ MD) and arterial oxygen saturation (Δ SaO_2) was accomplished with linear correlation and regression analyses. The difference in individual parameters was tested using the Wilcoxon signed-rank test. $P < 0.05$ was considered to be statistically significant.

Results

The demographic data of the 14 patients are summarized in Table I. Two patients (no. 1 and 3) were excluded from the analysis of PVF because pulsed Doppler PVF velocity tracings could not be obtained four minutes after phenylephrine *iv*. Phenylephrine *iv* significantly increased arterial blood pressure, central venous pressure, PaO_2, and SaO_2 (Table II). In the echocardiographic analysis, peak D increased significantly from 44.1 ± 14.9 to 56.7 ± 16.3 cm·sec^{-1}, where-

as peak S and peak R did not change significantly (from 35.4 ± 10.1 to 39.6 ± 13.7 cm·sec^{-1} and from 10.6 ± 5.2 to 9.0 ± 6.4 cm·sec^{-1}, respectively). Phenylephrine significantly increased both TVI-S and TVI-D, resulting in significant increases in TTVI (Table II). As a result, although heart rate decreased, the MD (TTVI × heart rate) increased significantly after phenylephrine (Table II). The correlation coefficient obtained between the changes in MD (% of baseline) and Δ SaO_2 were significant (n = 12, r = 0.72, Figure 2).

Discussion

It has been reported that systemic hypertension increases,[1–5] while hypotension decreases[2] arterial oxygenation in patients with tetralogy of Fallot. Using epicardial echocardiography with colour-flow imaging, Greeley *et al.*[7] reported that, in a child with tetralogy of Fallot, the decrease in blood pressure induced a marked reduction in SaO_2 and a net right-to-left shunt through the ventricular septal defect, while phenylephrine 25 µg *iv* restored SaO_2 and a reversal of shunting with a net left-to-right ventricular shunt. However, we are unaware of any prospective study demonstrating the relationship between arterial blood pressure and PBF in tetralogy of Fallot.

In the current study, phenylephrine significantly increased both arterial pressure and the MD. Additionally, there was a significant correlation (r = 0.72) between the change in the MD and the change in SaO_2. These results indicate that a phenylephrine-induced increase in arterial blood pressure increases PBF which is associated with the improvement of arterial oxygenation. It is likely that the reduction of right-to-left shunt produced by the increase in systemic vascular resistance is involved in the mechanisms of a phenylephrine-induced increase in PBF in tetralogy of Fallot. The results further suggest that PBF is a determinant of arterial oxygenation in tetralogy of Fallot.

The measurements of PVF velocity were accomplished in the left upper pulmonary vein in the present study. Therefore, the absolute value of PBF in children with tetralogy of Fallot cannot be evaluated. We previously reported that there was a good correlation between PBF measured by using a thermodilution technique and the MD in the left upper pulmonary vein in adult patients.[8] Although pulmonary circulation in children with tetralogy of Fallot is quite different from that in adult patients, we believe that assessment of the relative change in PBF is appropriate in the present study, because PVF velocity tracings were always obtained from the same branch (left upper pulmonary vein).

In summary, a phenylephrine-induced increase in arterial blood pressure produced a significant increase in MD and improvement of arterial oxygenation in children with tetralogy of Fallot, suggesting that arterial blood pressure is a determinant of PBF and arterial oxygenation in these patients.

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