Haemodynamic changes during induced hypotension – comparison of trimethaphan with prostaglandin E_1 assessed using transoesophageal echocardiography

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Haemodynamic changes during induced hypotension depend upon the hypotensive agent used. We investigated if, using transoesophageal echocardiography (TEE), we could identify the haemodynamic differences between trimethaphan and prostaglandin E_1 . Twenty-nine patients undergoing total hip replacement were selected for study. Hypotension was induced to a mean arterial pressure of 8.0–9.3 kPa with either trimethaphan ($5\text{--}20\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) or prostaglandin E_1 ($0.5\text{--}2.0\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). The left atrial dimension, cardiac output, fractional shortening, pulmonary venous flow and mitral valve flow were evaluated using TEE. During induced hypotension, left atrial dimension decreased in both trimethaphan and prostaglandin E_1 groups ($P < 0.05$). In the trimethaphan-treated patients systolic velocity in pulmonary venous flow decreased from $41.9 \pm 4.8\ \text{cm}\cdot\text{sec}^{-1}$ before induced hypotension to $27.8 \pm 4.2\ \text{cm}\cdot\text{sec}^{-1}$ by 30 min after stable hypotension had been established ($P < 0.01$). The late/early ratio of peak velocity in mitral blood flow decreased in prostaglandin E_1 treated patients. Cardiac output increased from $4.2 \pm 0.5\ \text{L}\cdot\text{min}^{-1}$ to

$5.3 \pm 0.4\ \text{L}\cdot\text{min}^{-1}$ during 30 min hypotension with prostaglandin E_1 administration ($P < 0.05$), but cardiac output decreased from 5.0 ± 0.5 to $3.5 \pm 0.4\ \text{L}\cdot\text{min}^{-1}$ with trimethaphan ($P < 0.01$). The differences in haemodynamic variables could be attributed to the venule dilatation effect of trimethaphan. We conclude that it was possible to detect the haemodynamic differences between trimethaphan and prostaglandin E_1 using TEE.

Les répercussions hémodynamiques de l'hypotension contrôlée dépendent de l'agent hypotenseur. Nous avons recherché si, avec l'échographie transoesophagienne (ETO) on pouvait identifier des différences entre les effets hémodynamiques du triméthaphan et de la prostaglandine E_1 . Vingt-neuf patients soumis à un remplacement total de la hanche sont inclus dans l'étude. La pression artérielle moyenne est abaissée à 8,0–9,3 kPa soit par le triméthaphan $5\text{--}20\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ soit avec par la prostaglandine E_1 ($0,5\text{--}2,0\ \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). La dimension auriculaire gauche, le débit cardiaque, la fraction de raccourcissement, le flux sanguin veineux et valvulaire mitral sont évalués par ETO. Pendant l'hypotension contrôlée, la dimension auriculaire gauche diminue avec le triméthaphan et la prostaglandine E_1 ($P < 0,05$). Dans le groupe triméthaphan, la vitesse systolique du flux veineux diminue de $41,9 \pm 4,8\ \text{cm}\cdot\text{sec}^{-1}$ avant l'hypotension à $27,8 \pm 4,2\ \text{cm}\cdot\text{sec}^{-1}$ 30 minute après l'accès au niveau de stabilité ($P < 0,01$). Le rapport entre le débit mitral de pointe tardif et précoce diminue avec la prostaglandine E_1 . Le débit cardiaque augmente de $4,2 \pm 0,5\ \text{L}\cdot\text{min}^{-1}$ à $5,3 \pm 0,4\ \text{L}\cdot\text{min}^{-1}$ pendant 30 min d'hypotension avec l'administration de prostaglandine E_1 ($P < 0,05$) mais diminue de $5,0 \pm 0,5$ à $3,5 \pm 0,4\ \text{L}\cdot\text{min}^{-1}$ avec le triméthaphan ($P < 0,01$). Les différences de variables hémodynamiques pourraient être causées par la dilatation des veinules par le triméthaphan. Nous concluons qu'il est possible de déceler les dif-

Key words

ANAESTHETIC TECHNIQUES: hypotension;

HORMONES: prostaglandin E_1 ;

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SYMPATHETIC NERVOUS SYSTEM: trimethaphan.

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férences hémodynamiques entre le triméthaphan et la prostaglandine E₁ par ETO.

Haemodynamic investigations during induced hypotension have been performed mainly with pulmonary artery catheterization. Transoesophageal echocardiography (TEE) is a noninvasive haemodynamic monitor used during anaesthesia and surgery. Pulmonary venous flow and left atrial dimension, which are not measurable with a pulmonary arterial catheter, can be estimated with TEE. However, there are few reports of haemodynamic investigations during induced hypotension with TEE.¹

The modes of action of trimethaphan and prostaglandin E₁ are different. Trimethaphan acts primarily on resistance and capacitance vessels, but prostaglandin E₁ dilates mainly resistance vessels, as does sodium nitroprusside.^{2,3} There is no report of a comparison of the haemodynamic differences of the two drugs in humans. We investigated if TEE could be used to detect the haemodynamic differences between two hypotensive agents.

Methods

The study was approved by the Ethics Committee of the institution and informed consent was obtained from each patient. Twenty-nine ASA 1–2 patients in whom total hip replacement was planned were the subjects in this study. In ten patients, hypotension was induced with trimethaphan and in 19 with prostaglandin E₁. Trimethaphan patients were studied first, followed to prostaglandin E₁ treated patients. During the study the same anaesthetists and orthopaedic surgeons were involved. Patients with hepatic, renal or endocrine diseases were excluded. The demography of the patients is shown in Table I.

Anaesthesia was induced with thiopentone 4 mg · kg⁻¹ and tracheal intubation was facilitated with succinylcholine 1 mg · kg⁻¹. Anaesthesia was maintained with enflurane (1.0–2.0%) in nitrous oxide (50%) and O₂ (50%). The lungs were ventilated to normocapnia with a Servo 900 C ventilator (Siemens). Hypotension was induced to a mean arterial pressure of 8.0–9.3 kPa with either trimethaphan (5–20 µg · kg⁻¹ · min⁻¹) or prostaglandin E₁ (0.5–2 µg · kg⁻¹ · min⁻¹) during the surgical procedure. Lactated Ringer's solution was infused at a rate of 6 ml · kg⁻¹ · min⁻¹. Blood losses were replaced with twice the volume lost with lactated Ringer's solution until Hct was reduced to 20% when blood transfusion was started.

The ECG, SaO₂, ETCO₂, central venous and arterial pressures were monitored throughout anaesthesia. Haemodynamic variables were monitored with TEE at the following times: before hypotension, 30 min and 60 min after stable hypotension had been obtained, and when the pre-hypotensive pressure had been re-established after

TABLE I Demographic data

	TMP group	PGE ₁ group
Age (yr)	51.0 ± 6.0	44.6 ± 4.1
Body weight (kg)	54.1 ± 2.3	51.4 ± 1.7
Height (cm)	153.3 ± 2.5	152.8 ± 2.2
Anaesth time (min)	251.0 ± 27.0	298.4 ± 22.4
Surg time (min)	197.8 ± 25.9	246.4 ± 21.0
Fluid in (ml)	2645 ± 228	3342 ± 278
Urine out (ml)	496 ± 146	600 ± 115

Mean ± SE. TMP: Trimethaphan. PGE₁: Prostaglandin E₁.

the cessation of hypotensive drug administration. Two-dimensional and pulse Doppler echocardiographic measurements were performed using an ultrasound system (Aloka SSD-870) equipped with 5 MHz 32-element transoesophageal single plane echoprobe (UST-5228S-5) and recorded on ½-inch videotape.

The anterior-posterior left atrial (LA) dimension was obtained during diastole. Cardiac output and fractional shortening were measured at left ventricular short axis. Cardiac output was calculated according to Pombo's method.⁴ Fractional shortening was measured to estimate left ventricular contractility. Mitral blood flow was estimated using the Doppler technique at the mitral valve and the late/early ratio of peak velocities (A/E) was determined: A/E was evaluated as the index of left ventricular diastolic function and preload. Systolic and diastolic velocity of pulmonary venous flow were measured at left upper pulmonary vein. Systolic velocity was evaluated to estimate the preload of left atrium.

One-way analysis of variance (ANOVA) for repeated measurements and Sheffe's F test were used to assess the effects of hypotensive agents. The unpaired t test was used to compare groups. *P* < 0.05 was considered to be statistically significant.

Results

The left atrial (LA) dimension was decreased during induced hypotension in both trimethaphan (*P* < 0.05) and prostaglandin E₁ groups (*P* < 0.01) (Table II). Systolic velocity of pulmonary venous flow decreased from 41.9 ± 4.8 cm · sec⁻¹ at pre-hypotension to 27.8 ± 4.2 cm · sec⁻¹ after 30 min of stable hypotension in the trimethaphan group (*P* < 0.01) but did not change in the prostaglandin E₁ group.

The late/early ratio of peak velocities in mitral blood flow (A/E) decreased after 60 min in the prostaglandin E₁ group (*P* < 0.05). In two patients in the prostaglandin E₁ group, we could not measure A/E due to the fusion of the A and E waves. Cardiac output decreased in the trimethaphan group (*P* < 0.01) and increased in the prostaglandin E₁ group (*P* < 0.05). No changes were seen

TABLE II Haemodynamic variables before, during and after induced hypotension

		<i>Hypotension</i>			
		<i>Before</i>	<i>30 min</i>	<i>60 min</i>	<i>After</i>
MAP (kPa)	TMP	11.5 ± 0.2	8.4 ± 0.2†	8.2 ± 0.2†	11.4 ± 0.3
	PGE1	10.8 ± 0.3	8.4 ± 0.2†	8.3 ± 0.2†	11.3 ± 0.3
HR (rpm)	TMP	72.8 ± 3.6	74.4 ± 5.1‡	77.3 ± 4.6‡	71.2 ± 5.1
	PGE1	81.6 ± 2.9	90.9 ± 2.3*	90.8 ± 3.1†	84.7 ± 3.4
CVP (kPa)	TMP	1.3 ± 0.1	1.0 ± 0.1†	1.0 ± 0.1†	1.2 ± 0.1
	PGE1	1.1 ± 0.1	0.8 ± 0.1†	0.8 ± 0.1†	1.0 ± 0.2
LA (cm)	TMP	2.6 ± 0.2	2.6 ± 0.2	2.2 ± 0.1*	2.5 ± 0.3
	PGE1	2.8 ± 0.1	2.4 ± 0.1†	2.4 ± 0.1*	2.7 ± 0.1
PS (cm · sec ⁻¹)	TMP	41.9 ± 4.8	27.8 ± 4.2†‡	32.9 ± 4.3*	36.9 ± 3.3
	PGE1	41.2 ± 5.3	42.8 ± 3.9	40.5 ± 2.3	46.8 ± 4.5
PD (cm · sec ⁻¹)	TMP	31.0 ± 5.5	31.7 ± 5.2	27.2 ± 3.0	27.1 ± 2.6
	PGE1	36.1 ± 5.4	36.1 ± 4.7	33.8 ± 3.7	39.9 ± 6.3
A/E (%)	TMP	89.5 ± 9.8	78.5 ± 6.9	90.6 ± 9.3	96.6 ± 15.5
	PGE1	77.2 ± 7.2	73.1 ± 8.1	65.0 ± 8.2*	80.9 ± 9.6
CO (L · min ⁻¹)	TMP	5.0 ± 0.5	3.5 ± 0.4†‡	3.6 ± 0.5*	4.6 ± 0.6
	PGE1	4.2 ± 0.5	5.3 ± 0.4*	4.8 ± 0.4	4.6 ± 0.6
FS (%)	TMP	31.8 ± 2.9	30.9 ± 1.9	37.0 ± 1.8	33.3 ± 3.7
	PGE1	31.1 ± 3.6	36.9 ± 3.1	36.5 ± 2.5	32.8 ± 4.9

Mean ± SE.

**P* < 0.05†*P* < 0.01 compared with before value.‡*P* < 0.05 compared between groups.TMP: Trimethaphan. PGE1: Prostaglandin E₁. MAP: Mean arterial blood pressure. LA: Left atrial dimension. PS: Systolic velocity of pulmonary venous flow. PD: Diastolic velocity of pulmonary venous flow. A/E: Late/early ratio of peak velocities in mitral blood flow. CO: Cardiac output.

FS: Fractional shortening.

in diastolic velocity in pulmonary venous flow and fractional shortening in left ventricle in both groups.

Discussion

Trimethaphan has been used widely as a hypotensive agent due to its potent and short duration of action. It blocks autonomic ganglia, and dilates resistance and capacitance vessels simultaneously. It decreases cardiac output, renal and hepatic blood flow, and increases muscle and skin flow. However, its use is limited by histamine release.²

Prostaglandin E₁ dilates arterioles through direct effects on vascular smooth muscle, and its ability to suppress vascular responsiveness to endogenous constrictor amines and polypeptides.⁵ It increases cardiac output and heart rate, and maintains renal, hepatic, and coronary flows.⁶

Fukuzaki *et al.*⁷ reported differences in coronary vascular resistance and ventricular contractility between two drugs in dogs. We found differences in systolic velocity of pulmonary venous flow, A/E and cardiac output in humans. Our finding can be explained by which vessels, resistance and/or capacitance ones, are dilated.

There were decreases in LA dimension in patients treated with prostaglandin E₁ or trimethaphan. Measurement of LA is used as the way of judging whether the chamber is dilated. The LA diameter obtained from TEE is said to be less than the diameter obtained from transthoracic echocardiography.⁸

Systolic velocity of pulmonary venous flow occurs during atrial relaxation for reduction of left atrial pressure⁹ and reflects well the left atrial pressure during cardiac surgery.¹⁰ Nitroglycerin reduces preload and decreases systolic velocity in pulmonary venous flow.¹¹ We found reduction of systolic velocity in the patients with trimethaphan, but not in the patients with prostaglandin E₁. The venous dilatation effect of trimethaphan may decrease preload and systolic velocity of the pulmonary venous flow.

Diastolic velocity of pulmonary venous flow is formed during left ventricular relaxation and rapid transmural filling of the ventricle. Administration of nitroglycerin does not change diastolic velocity.¹² Neither trimethaphan or prostaglandin E₁ affected it in our study.

The late/early ratio of peak velocity in mitral blood flow (A/E) reflects diastolic function of the left ventricle.

In patients with reduced compliance, the early diastolic flow is diminished and A/E is also reduced. In addition, A/E reflects preload and administration of nitroglycerin decreased preload and increases A/E. In this study, A/E decreased with prostaglandin E_1 but not with trimethaphan. The potent venous dilatation effect of trimethaphan may explain the increase of A/E compared with prostaglandin E_1 .

Heart rate changes affect the ratio of A/E.¹³ Despite the heart rate increase, patients with prostaglandin E_1 did not show an increase of A/E. In addition to heart rate, there are several factors that affect A/E value such as: (1) left atrial compliance, (2) left atrial contractile state, (3) pulmonary venous return, (4) mitral valve function, (5) left chamber stiffness, (6) external constraints, (7) the phase of the respiratory cycle.^{14,15} We could not tell which factor played the most important role during the induced hypotension with prostaglandin E_1 .

The cardiac output was calculated by measuring left ventricular volume at short axis. The short axis measurement from TEE is well correlated with that from transthoracic echocardiography.⁸ The calculation of stroke volume in echocardiography has limitation if patients have wall motion abnormality.¹⁶ No patients in our study showed abnormal ventricular contraction.

Fractional shortening describes the quality of ventricular contraction. Nakano *et al.*¹⁷ reported that prostaglandin E_1 had a positive inotropic effect and enhanced the isometric tension (dp/dt). Trimethaphan was reported to depress dp/dt in dogs.⁷ However, in this study we could not find any changes in fractional shortening during trimethaphan and prostaglandin E_1 administration. We can not eliminate the effect of enflurane anaesthesia on myocardial contractility.

Transoesophageal echocardiography is being widely used mainly in cardiac anaesthesia to estimate myocardial wall ischemia and ventricular function. We established differences in haemodynamic variables between trimethaphan and prostaglandin E_1 in patients during induced hypotension using TEE.

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