CARDIOVASCULAR HAEMODYNAMICS AFTER INDUCTION OF ANAESTHESIA WITH ALTHESIN IN PATIENTS WITH VALVULAR HEART DISEASE

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ALTHESIN may produce myocardial depression and hypotension.^{1,2} Experiments performed on animals have shown that the therapeutic index of Althesin (i.e., the ratio of the lethal dose in 50 per cent of experimental animals to the dose which produces anaesthesia in 50 per cent of the animals) is four times that of thiopentone and 3½ times that of ketamine.³ In addition, Althesin has been shown to depress sympathetic tone but nevertheless causes tachycardia through a vagolytic effect.² Althesin has been shown to cause cardiovascular depression in patients with valvular heart disease when administered together with pancuronium.⁴ We present the details of a haemodynamic study of the cardiovascular actions of Althesin when used for induction in patients with cardiac valvular disease.

MATERIALS AND METHODS

Eight patients with valvular heart disease scheduled for mitral and/or aortic valve replacement were studied. The experimental protocol was approved by the chairmen of the Department of Anaesthesia and the Department of Cardiothoracic surgery. Informed consent for the study was obtained from all patients participating in this study. Detailed information about the risks of both anaesthesia and surgery was given to all patients as is the usual practice of the cardiac surgical team. Mean age of the patients was 55 years (range 33–66). Six patients suffered from aortic valve disease and underwent aortic valve replacement. One patient suffered from both aortic and mitral valvular disease and underwent double valve replacement; and one patient needed mitral valve replacement only. The preoperative mean cardiac index obtained at cardiac catheterization was 2.4 l/min·m² (range 1.8–3.2). Five patients were in functional group

II, and three in functional group III, according to the New York Heart Association (N.Y.H.A.) classification.

Premedication consisted of diazepam 0.1 mg·kg⁻¹ and scopolamine 0.005 mg·kg⁻¹ given intramuscularly two hours before induction of anaesthesia to assure adequate sedation. Under local anaesthesia a radial artery was cannulated, a Swan-Ganz flow directed thermodilution catheter was inserted through the right internal jugular vein by a percutaneous technique⁵ and a central venous catheter was inserted from a cubital vein for drug injection.

The following parameters were recorded before induction of anaesthesia with Althesin 0.1 ml·kg⁻¹ given intravenously and in the period from three to five minutes after loss of consciousness: mean arterial pressure (MAP), central venous pressure (CVP), pulmonary arterial mean pressure (PAMP), pulmonary capillary wedge pressure (PCWP), using Siemens transducers positioned at the midaxillary line of the patient placed supine on the operating table. Since the plasma half-life of Althesin in animals has been shown to be only eight minutes,³ we elected to make only one set of measurements. Heart rate was counted from the pulse curve. The electrocardiogram and the parameters mentioned above were recorded on a 6-channel recorder (Mingograph, Elema-Schoenander). Cardiac output was measured by the thermodilution method by a cardiac output computer (model 9510, Edwards).⁶ The mean of two cardiac output measurements was used for calculations. Cardiac index (CI) and stroke index (SI) were calculated using the height and weight nomogram of DuBois.⁷ Systemic vascular resistance (SVR), pulmonary vascular resistance (PVR) were calculated together with mean arterial pressure and pulmonary arterial mean pressure from the formulae shown in the appendix. Blood samples were drawn from the arterial catheter and analyzed for Po₂, Pco₂ and pH, using an automatic blood gas analyzer (ABL2, Radiometer).

Althesin was injected slowly over a period of 20 to 30 seconds. During the control period the patients breathed 100 per cent oxygen delivered by

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TABLE 1

HAEMODYNAMIC EFFECTS OF ALTHESIN-OXYGEN ANESTHESIA IN EIGHT PATIENTS WITH VALVULAR HEART DISEASE. THE VALUES ARE MEANS $\pm$ 1 STANDARD ERROR. A SIGNIFICANT CHANGE IS EXPRESSED BY A P-VALUE

	Preanaesthetic values	Anaesthetic values	p-values
Heart rate (beats/min)	69 $\pm$ 4.4	86 $\pm$ 4.0	<0.01
Stroke index (ml/m ²)	33 $\pm$ 3.9	28 $\pm$ 2.3	<0.01
Cardiac index (l/min·m ²)	2.11 $\pm$ 0.22	2.34 $\pm$ 0.21	
Mean arterial pressure (kPa)	12.3 $\pm$ 2.3	10.7 $\pm$ 1.7	
Central venous pressure (kPa)	0.9 $\pm$ 0.1	0.8 $\pm$ 0.2	
Pulmonary arterial mean pressure (kPa)	3.4 $\pm$ 0.4	2.6 $\pm$ 0.2	
Pulmonary capillary wedge pressure (kPa)	2.6 $\pm$ 0.3	2.1 $\pm$ 0.2	
Pulmonary vascular resistance (kPa·sec/l)	12.3 $\pm$ 2.6	7.7 $\pm$ 1.4	<0.05
Systemic vascular resistance (kPa·sec/l)	153.2 $\pm$ 18.3	168.6 $\pm$ 30.2	
Acid-base measurements			
PaO ₂ (kPa)	51.6 $\pm$ 1.2	52.5 $\pm$ 2.5	
Paco ₂ (kPa)	4.8 $\pm$ 0.2	5.4 $\pm$ 0.2	
pH	7.412 $\pm$ 0.012	7.387 $\pm$ 0.013	

face mask for 4 to 5 minutes before measurements were done. If respiration was judged clinically to be depressed after induction with Althesin, ventilation was assisted manually using a semi-open circle system with an oxygen flow of 10 l/min. All measurements were done before tracheal intubation and operation. Statistical analyses were done by paired t-tests. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The results are shown in Table 1.

Heart rate increased from 69 $\pm$ 4.4 to 86 $\pm$ 4.0 beats/min ($p < 0.01$), but stroke index declined from 33 $\pm$ 3.9 to 28 $\pm$ 2.3 ml/m² ($p < 0.01$). Mean arterial pressure and cardiac index were unaffected. Pulmonary vascular resistance declined from 12.3 $\pm$ 2.6 to 7.7 $\pm$ 1.4 kPa·sec/l ($p < 0.05$). All other measured parameters as well as systemic vascular resistance were unaffected. It should be noted that neither PaO₂ nor Paco₂ changed when pulmonary vascular resistance declined.

DISCUSSION

Premedication was given two hours before the study. Diazepam was used for its excellent sedative and minor cardiovascular effects;⁸ scopolamine was chosen for its minimal influence on the heart rate.⁹

Our findings are in contrast to those of Harrison and Sellick,⁴ who found a severe drop in arterial blood pressure in patients presenting for open-heart surgery after induction with Althesin

0.05 ml·kg⁻¹. These authors found a decrease in arterial blood pressure of more than 40 per cent which was associated with considerable tachycardia. However, in their study, the patients received pancuronium 8 mg intravenously immediately after the induction dose of Althesin, and ventilation was controlled with 50 per cent nitrous oxide in oxygen. Pancuronium has been shown to cause an increase of heart rate due to a vagolytic action.¹⁰ Patients with valvular heart disease are known to respond to excessive tachycardia with decreased cardiac function, even heart failure, resulting in a severe fall in blood pressure. It is therefore reasonable that the blood pressure decline observed by Harrison and Sellick⁴ was due in part to the vagolytic action of pancuronium and the depressant action of nitrous oxide.

Sapthavichaiikul, *et al.*² warn against the clinical use of Althesin in situations where blood pressure is maintained by high sympathetic tone, as in patients with severe cardiac disease, since Althesin severely depresses sympathetic activity and has a vagolytic action. Sapthavichaiikul, *et al.* conducted their study in cats and based their conclusions not only on their own observations but in part on the study done by Harrison and Sellick, and both studies are contradicted by our findings. Prys-Roberts *et al.*¹¹ demonstrated a 24 per cent increase in heart rate and a 15 per cent decrease in blood pressure after Althesin 0.05 ml·kg⁻¹ in hypertensive patients. We found a 20 per cent increase in heart rate, but no significant fall in blood pressure and no significant changes in cardiac output or systemic vascular resistance.

According to the study of Saphthavichaiikul, *et al.*² a fall in systemic vascular resistance should occur due to vasodilation from decrease in sympathetic tone. Doenicke, *et al.*¹² have demonstrated that Althesin releases histamine in various degrees, which should also tend to decrease systemic vascular resistance. Other investigators (Coleman, *et al.*¹³) have also found a fall in systemic vascular resistance after Althesin. Our findings and those of Prys-Roberts, *et al.*¹¹ are contrary to these.

We found a significant reduction of pulmonary vascular resistance of 27 per cent after Althesin, a change that cannot be explained by changes in blood gas tensions.

Few studies have examined the effect of Althesin on the pulmonary circulation in man. In six patients studied during diagnostic heart catheterization, Campbell, *et al.*¹⁴ could demonstrate no change in pulmonary artery mean pressure except in cases with mitral stenosis, where a slight increase occurred. Similarly Rifat, *et al.*¹⁵ found no change in pulmonary artery pressure after Althesin 0.07 mg·kg⁻¹. Wedge pressures were not measured in the above-mentioned studies.^{13,14}

Our results indicate vasodilating effects of Althesin on the pulmonary circulation, the cause of which deserves further studies. Foëx and Prys-Roberts¹⁶ found a dose-related increase in pulmonary vascular resistance in goats after Althesin administration, which was possibly due to alveolar hypoventilation. Further studies, therefore, are necessary in man to elucidate the mechanism of action of Althesin on the pulmonary vascular resistance.

On the basis of our findings we conclude that Althesin given intravenously in a dose of 0.1 ml·kg⁻¹ to patients with valvular heart disease is associated with only minimal cardiovascular depression and a decrease in pulmonary vascular resistance that may even be advantageous.

SUMMARY

The haemodynamic effects of the induction of anaesthesia with Althesin 0.1 ml·kg⁻¹ were studied in eight patients with valvular heart disease before tracheal intubation and surgery. A 20 per cent reduction in stroke index was compensated for by an increase in heart rate of similar magnitude. Cardiac index, mean arterial, pulmonary arterial, central venous and pulmonary

capillary wedge pressures and systemic vascular resistance were unaffected. Pulmonary vascular resistance declined by nearly 30 per cent. It is therefore concluded that Althesin causes only minimal cardiovascular depression in patients with valvular heart disease.

RÉSUMÉ

On a évalué l'Althésin comme agent d'induction à la dose de 0.1 ml/kg chez huit patients porteurs de cardiopathies valvulaires; les observations ont été faites avant l'intubation et la chirurgie. La diminution de 20 pour cent de l'index d'éjection que nous avons observée était compensée par une élévation de la fréquence cardiaque du même ordre. L'index cardiaque, la pression artérielle moyenne, la pression veineuse centrale, la pression capillaire bloquée, ainsi que la résistance vasculaire périphérique n'étaient pas modifiés. On a observé une diminution de 30 pour cent de la résistance vasculaire pulmonaire. Les auteurs concluent que l'Althésin ne produit qu'une dépression cardiovasculaire minime chez les patients présentant une cardiopathie valvulaire.

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APPENDIX

Symbols and Abbreviations

HR:	heart rate (beats/min).
CO:	cardiac output (l/min).
CI:	cardiac index (l/min · m ²)
SI:	stroke index (ml/m ²).
CVP:	central venous pressure (mm Hg ~ 0.133 kPa).
PAMP:	pulmonary arterial mean pressure (mm Hg ~ 0.133 kPa).
PCWP:	pulmonary capillary wedge pressure (mm Hg ~ 0.133 kPa).
MAP:	systemic mean blood pressure (mm Hg ~ 0.133 kPa).
PVR:	pulmonary vascular resistance (dynes · sec · cm ⁻⁵ ~ 0.1 kPa · s/l).
SVR:	systemic vascular resistance (dynes · sec · cm ⁻⁵ ~ 0.1 kPa · s/l).
PaO ₂ :	arterial oxygen tension (mm Hg ~ 0.133 kPa).
PaCO ₂ :	arterial carbon dioxide tension (mm Hg ~ 0.133 kPa).

Formulae

MAP:	diastolic pressure + 1/3 of the pulse amplitude (mm Hg ~ 0.133 kPa).
PAMP:	diastolic pressure + 1/3 of the pulse amplitude (mm Hg ~ 0.133 kPa).
CI	= CO/body surface area (l/min · m ²).
SI	= CI 1000/HR (ml/m ²).
PVR	= (PAMP – PCWP) × 80/CO (dynes · sec · cm ⁻⁵ ~ 0.1 kPa · s/l).
SVR	= (MAP – CVP) × 80/CO (dynes · sec · cm ⁻⁵ ~ 0.1 kPa · s/l).

Conversion factor: 1 kPa = 7.5 mm Hg.