The haemodynamic effects of subcutaneous sumatriptan, a 5HT₁-receptor agonist

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Aims Previous *in vivo* studies with sumatriptan, a 5HT₁-receptor agonist, have demonstrated vasopressor responses in the pulmonary and systemic arterial circulation. Pulmonary artery wedge pressure (PAWP) also increases after sumatriptan injection, raising the possibility of an additional venoconstrictive action or a negative inotropic effect. The mechanism for the rise in PAWP was investigated in the study.

Methods Ten patients undergoing diagnostic coronary arteriography underwent haemodynamic monitoring.

Results There was a significant rise ($P < 0.05$) in systemic and pulmonary arterial pressure and total systemic and pulmonary vascular resistance. There was a similar rise ($P < 0.05$) in PAWP and left ventricular end diastolic pressure (LVEDP). There was no change in cardiac output nor in peak rate of left ventricular pressure rise (dP/dt).

Conclusions The sumatriptan induced rise in PAWP and LVEDP appears consequent upon increased afterload although a negative inotropic effect cannot be excluded.

Keywords: sumatriptan, 5-hydroxytryptamine, vasoconstriction, haemodynamics

Introduction

Sumatriptan, is a selective 5HT₁-receptor agonist effective in the acute treatment of migraine [1, 2]. Previous *in vivo* studies with sumatriptan have demonstrated vasopressor responses in the systemic and pulmonary circulation with an additional rise in pulmonary artery wedge pressure (PAWP) [3, 4]. The increase in PAWP was postulated to be secondary to pulmonary venoconstriction but direct measurement of the left atrium or left ventricular end diastolic pressure was not made to exclude a rise in PAWP due to a reduction in left ventricular contractile function. In order to investigate this further, we assessed the effects of a standard dose of sumatriptan (6 mg s.c.) on standard haemodynamic parameters including simultaneous measurement of the PAWP and LVEDP and on inotropic effects by measuring the peak rate of left ventricular pressure rise (dP/dt).

Methods

Ten patients (3M:7F—aged 49 ± 9 years) were studied following the conclusion of diagnostic coronary arteriography. All vasoactive therapy was discontinued 24 h before study. Patients with recent (within 3 months) myocardial infarction or unstable angina, hypertension (diastolic BP > 95 mmHg), a history of migraine and women of child-bearing potential were excluded from the study. Patients found to have coronary artery stenosis of $> 50\%$ during diagnostic angiography were not entered. The study was approved by the Ethics committee of the Western Infirmary.

Each patient was issued an appropriate information sheet and written informed consent was obtained.

Haemodynamic monitoring

After the diagnostic procedure, a pigtail catheter was employed to measure systemic arterial and left ventricular pressure. A left ventricular pressure tracing was expanded to 100 mm s^{-1} and digitised to allow the calculation of peak rate of rise of pressure (dP/dt). Right atrial, pulmonary artery and pulmonary artery wedge pressures were measured with a Swan Ganz catheter. Cardiac output was measured by the thermodilution technique. Hard copy ECGs and pressure tracings were recorded at 10 min intervals, following placebo and sumatriptan (6 mg) subcutaneous injection. As drug administration was single-blinded, pressure tracings and ECGs were analysed by a blinded observer.

Results

As shown in Table 1 and Figure 1, there were significant changes ($P < 0.05$ ANOVA) in systemic (SVR) and pulmonary vascular resistance (PVR), right atrial pressure (RAP, PAWP and LVEDP). No significant change was observed in heart rate (HR), cardiac output (CO) or dP/dt.

Discussion

These results confirm 5HT₁ mediated vasoconstriction in the pulmonary and systemic circulation following a standard clinical dose of sumatriptan. Pulmonary artery wedge pressure increased from 6 mmHg to 9.3 mmHg (55%) in the present study, compared with the 80% increase (8.7 mmHg to 15.6 mmHg) previously observed [4].

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Table 1 The results of the study.

	Time post sumatriptan			Statistical significance (*)
	Placebo	10 min	20 min	
HR	65.6 ± 10.84	65.1 ± 7.86	63.1 ± 7.49	P=NS
SVR (dyn s cm ⁻⁵)	1456 ± 396	1672 ± 479*	1726 ± 394*	P<0.01
PVR (dyn s cm ⁻⁵)	119 ± 38	142 ± 47*	143 ± 47*	P<0.05
RAP (mmHg)	4.3 ± 2.7	4.5 ± 2.5	6.3 ± 2.2*	P<0.01
PAWP (mmHg)	6.0 ± 2.6	7.9 ± 2.8*	9.3 ± 2.4*	P<0.02
LVEDP (mmHg)	7.3 ± 2.6	12.0 ± 4.3*	12.1 ± 2.4*	P<0.001
CO (l min ⁻¹)	4.8 ± 1.4	4.8 ± 1.3	4.7 ± 1.0	P=NS
dP/dt (mmHg s ⁻¹)	2151 ± 734	2323 ± 918	1962 ± 936	P=NS

Figure 1 PAWP (■) and LVEDP (□) pressure changes after sumatriptan injection (mean ± s.d.). +P<0.001; *P<0.05.

Simultaneous measurement of the LVEDP showed a rise of a similar degree to the pulmonary artery wedge pressure and it may be that the change in the occluded wedge pressure is a reflection of this rise rather than a pulmonary venoconstrictive effect. The rise in LVEDP could be secondary to increased after load or reflect a negative inotropic effect. A negative inotropic effect has not previously been noted with serotonergic agonists and studies with human ventricular muscle preparations show a lack of functional 5HT receptors in terms of contractile effects [5, 6]. Human atrial preparations, however, elicit a 5HT₄ mediated positive inotropic effect [6]. It is therefore possible that the rise in LVEDP is consequent upon increased after load. The minor non significant reduction in the rate of rise of isovolumic pressure (dP/dt) could therefore reflect the ventricular response to raised aortic pressure and is very unlikely to be of clinical significance.

The acute increase in pulmonary artery pressure seen in this study would be expected to raise right ventricular end diastolic pressure and through this mechanism may therefore account for the observed elevation in right atrial pressure.

The relative percentage increase in RAP, however, exceeded the change in PAP approximately two-fold raising the possibility that part of the rise in right atrial pressure may reflect systemic venoconstriction in addition to pulmonary artery vasoconstriction. Data on 5HT receptor distribution and density in the human circulation is presently scarce, however, and these conclusions remain speculative.

In summary, a standard dose of 6 mg sumatriptan, subcutaneously, increased left ventricular end diastolic pressure and pulmonary artery wedge pressure with no effect on peak rate of left ventricular pressure rise. An additional venoconstrictive action remains a possibility, but requires further investigation.

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