Br. J. clin. Pharmac. (1989), **28**, 89S–91S

Effects of xamoterol on sodium excretion in volunteers

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Xamoterol has been shown to reduce the frequency of oedema and lung crepitations in heart failure. We examined its effects on blood pressure and renal function in healthy volunteers. Systolic blood pressure rose, sodium and chloride excretion increased and there was a strong correlation in individual subjects between rises in systolic blood pressure and in sodium excretion. Although no changes in glomerular filtration rates were seen, changes sufficient to explain the observed rise in sodium excretion are well within the experimental error of this study. Xamoterol may increase sodium excretion by an action on renal haemodynamics.

Keywords xamoterol sodium excretion renal function

Introduction

It was demonstrated in the German and Austrian Xamoterol Study Group trial (1988) that xamoterol reduced peripheral oedema and basal crepitations in the lung. This could not be accounted for by changes in diuretic treatment, which remained constant throughout the course of this study. It is conceivable that salt and water excretion could be promoted by the effects of xamoterol on haemodynamics. We examined the effects of xamoterol on renal function in normal volunteers.

Methods

Ten healthy volunteers (five males, five females) with an average age of 30.2 years (range 24–45) were each given a single intravenous dose of xamoterol 0.2 mg kg^{-1} or placebo. Each subject underwent two studies, 2 weeks apart in random order. Measurements were made in the supine position of heart rate, blood pressure, renal blood flow, glomerular filtration rate, creatinine clearance, urine volume and free water clearance at different times as shown in Figure 1. The excretion of sodium, chloride and potassium was also measured. The study was approved by the Ethics Committee of the University and Hospital of Lyon.

Results

The effects of xamoterol and placebo on the variables measured are shown in Table 1. Xamoterol caused significant rises in the excretion of sodium (Figure 2) and chloride with no change in potassium excretion. There were small increases in renal blood flow (PAH clearance), creatinine clearance and urine volume, but these were not statistically significant. Heart rate rose from 64 to 70 beats min^{-1}, and systolic blood pressure from 112 to 124 mm Hg. Figure 3 shows the relationship between sodium excretion and systolic blood pressure in seven patients. In individual patients there was a correlation (r = 0.9) between the increase in systolic blood pressure and that in sodium excretion.

Discussion

Xamoterol had a significant effect on renal sodium excretion which was not explained by alterations in plasma electrolytes, aldosterone, renin or protein values (which remained unchanged). On the other hand, xamoterol increased systolic blood pressure and there was a strong correlation between the changes in blood pressure and in sodium excretion. The explanation for this could be that the higher systolic blood pressure caused

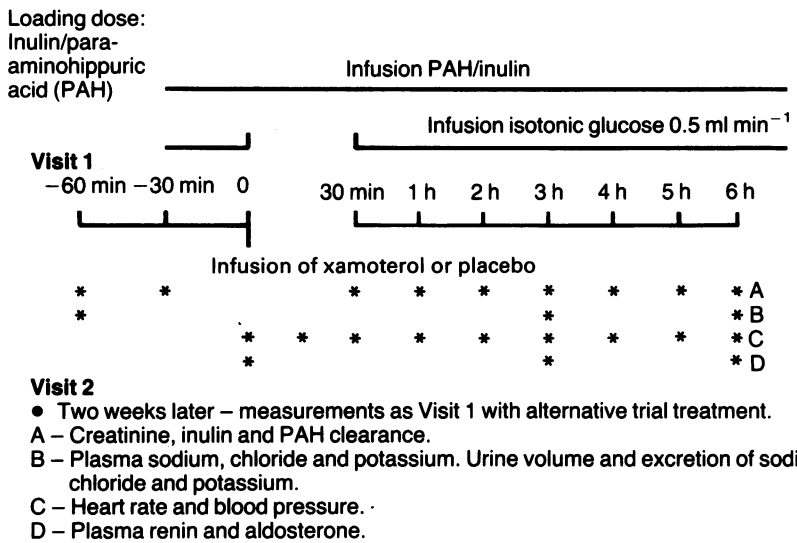

Figure 1 Experimental protocol.

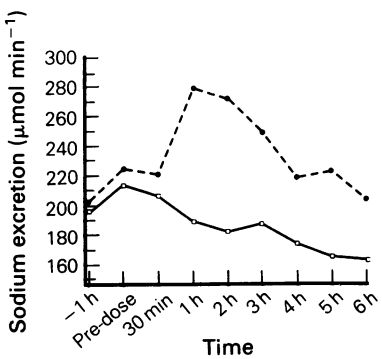

Figure 2 Means of sodium excretion (μmol min^{-1}) after placebo (□) and xamoterol (●).

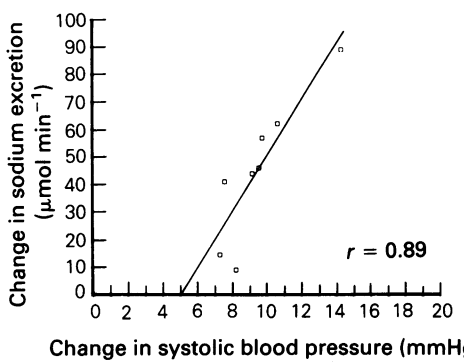

Figure 3 Correlation between sodium excretion and systolic blood pressure (n = 7).

Table 1 Blood pressure, heart rate and renal function after intravenous xamoterol and placebo

	Xamoterol	*Placebo*
Heart rate (beats min^{-1})	69.8 ± 1.2*	63.6 ± 1.2
Systolic blood pressure (mm Hg)	124.4 ± 1.6*	112.3 ± 1.6
Diastolic blood pressure (mm Hg)	67.1 ± 1.4	65.4 ± 1.4
PAH clearance (ml min^{-1}) (RBP)	693.4 ± 12.5	663.4 ± 12.5
Inulin clearance (ml min^{-1}) (GFR)	120.7 ± 2.3	119.9 ± 2.3
Creatinine clearance (ml min^{-1})	120.1 ± 2.9	111.3 ± 2.9
Sodium excretion (μmol min^{-1})	235.8 ± 5.7*	183.4 ± 5.7
Chloride excretion (μmol min^{-1})	249.5 ± 20.0**	165.0 ± 20.0
Potassium excretion (μmol min^{-1})	63.7 ± 4.3	61.6 ± 4.3
Osmolar clearance (ml min^{-1})	4.7 ± 0.1**	4.2 ± 0.1
Free water clearance (ml min^{-1})	−2.5 ± 0.1	−2.3 ± 0.1
Urine flow (ml min^{-1})	2.2 ± 0.1	1.9 ± 0.1

*$P < 0.01$, **$P < 0.005$

a small rise in glomerular filtration rate. In this study, measurements of inulin or creatinine clearances did not reveal statistically significant differences in glomerular filtration rate, but the rise in sodium excretion could be explained by an increase in glomerular filtration rate of only 1 ml min^{-1}, which is well within the error of measurements in this study (O'Connor, 1982). However, this is speculative. It is possible that in patients with heart failure the positive inotropic effects of xamoterol might produce a lower incidence of fluid retention through some mechanism involving a change in renal haemodynamics. Further studies are now in progress in heart failure patients with signs of fluid retention to investigate this in more detail.

References

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