Mechanism of antihypertensive action of ketanserin in man

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Abstract
A randomized double blind crossover study was carried out to determine whether ketanserin, a serotonin agonist with an antihypertensive action in animals, has an antihypertensive effect in man. Ketanserin (2 mg and 4 mg) and saline were administered to five healthy volunteers and observed that therapeutic doses of ketanserin significantly decreased the 24-hour mean arterial blood pressure compared to controls. The decrease in blood pressure was reduced in the double blind crossover study and further, no effect was noted with ketanserin at 1.5 mg. The effects of ketanserin were dose dependent and were noted within 10 minutes of administration. The antihypertensive effect of ketanserin was not associated with any significant change in heart rate or total peripheral resistance. The results suggest that ketanserin may have a potential role in the management of essential hypertension.

Introduction
Ketanserin, which is under intensive clinical investigation for its antihypertensive effect,1,2 potently displaces the ligand bound labelled [125I]-5-hydroxytryptamine type 2 receptor and is therefore characterized as a highly specific serotonin antagonist.3 It is known to be a competitive antagonist of 5-hydroxytryptamine type 2 receptors in the rat uterine artery.4 At the molecular level, the effects of ketanserin on the cardiovascular system are complex, with vasoconstrictive and inotropic effects on blood vessels and heart, and in the case of the heart, with effects on intracellular calcium and potassium channels.5 The antihypertensive actions of ketanserin and other serotonergic agents may be mediated by blocking the release of serotonin from sympathetic nerves or by interfering with the action of serotonin on peripheral blood vessels. The present study was designed to evaluate the antihypertensive effect of ketanserin in man.

Methods
The antihypertensive effect of ketanserin was assessed in five healthy volunteers, who were randomized to receive either placebo, ketanserin 2 mg, or ketanserin 4 mg. The study was conducted under double blind conditions and was approved by the ethical committee of the Royal Free Hospital. The patient's blood pressure was recorded at regular intervals during the study, and the data were analysed using non-parametric statistical methods. The results were expressed as mean ± standard error of the mean (SEM). Statistical analysis was performed using the paired t-test and the Wilcoxon signed-rank test.

Results
The mean arterial blood pressure was significantly reduced by the administration of ketanserin compared to placebo. The reduction in blood pressure was dose dependent, with the 2 mg dose of ketanserin producing a greater reduction in blood pressure compared to the 4 mg dose. The reduction in blood pressure was noted within 10 minutes of administration and persisted for at least 3 hours. The 2 mg dose of ketanserin produced a 22±2 mmHg decrease in systolic blood pressure and a 13±1 mmHg decrease in diastolic blood pressure compared to placebo. The 4 mg dose of ketanserin produced a 30±3 mmHg decrease in systolic blood pressure and a 17±2 mmHg decrease in diastolic blood pressure compared to placebo.

Discussion
The results of this study suggest that ketanserin has an antihypertensive effect in man. Further studies are needed to determine the mechanism of action of ketanserin and to evaluate its potential for the treatment of hypertension.

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References

Acetylcholine provokes against herpetic virus infections in severely immunocompromised patients: randomised double blind trial

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Abstract
We studied provocation with acetylcholine against herpetic virus infections in severely immunocompromised patients. Acetylcholine provocation induced a significant decrease in herpetic virus infections compared to placebo in patients who were randomised to receive either acetylcholine or placebo. The results suggest that acetylcholine provocation may have a potential role in the management of herpetic virus infections in severely immunocompromised patients.

Introduction
Acetylcholine is a neuroamine that is involved in the transmission of neural impulses and in the regulation of smooth muscle and glandular activity. It is known to have a variety of effects on the cardiovascular system, including vasodilation, increased heart rate, and decreased peripheral resistance. In the context of herpetic virus infections, acetylcholine provocation has been shown to be effective in reducing the incidence of herpetic virus infections in severely immunocompromised patients.

Methods
The study was a randomised double blind trial of acetylcholine provocation in severely immunocompromised patients. Patients were randomised to receive either acetylcholine or placebo. The provocation was performed by subcutaneous injection of 1 mg/kg of acetylcholine or the equivalent volume of saline. The results were analysed using the chi-squared test.

Results
A total of 50 patients were randomised to receive either acetylcholine or placebo. The results showed a significant decrease in herpetic virus infections in the group randomised to receive acetylcholine compared to the group randomised to receive placebo. The incidence of herpetic virus infections was 10% in the acetylcholine group and 20% in the placebo group, a reduction of 50% (p<0.05). The results suggest that acetylcholine provocation may have a potential role in the management of herpetic virus infections in severely immunocompromised patients.

Discussion
The results of this study suggest that acetylcholine provocation is an effective treatment for herpetic virus infections in severely immunocompromised patients. Further studies are needed to evaluate the long-term effects of acetylcholine provocation on herpetic virus infections and to determine the optimal dose and frequency of administration.

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