EFFECT OF PENTAZOCINE ON RENAL BLOOD FLOW

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SUMMARY
Twenty dogs (weight 8-14 kg) were anaesthetized with sodium pentobarbitone 25 mg per kg body weight and anaesthesia was maintained with nitrous oxide in oxygen. Respiration was controlled with a volume-limited respirator (PaCO₂ 4.7 ± 0.4 kPa). Renal blood flow was measured with a square wave electromagnetic flow meter inserted through a left paramedian laparotomy. Renal blood flow decreased transiently following an i.v. injection of pentazocine. The decreases were 81% ± 10.8 and 77% ± 3 of the control following the administration of pentazocine 1 mg and 2 mg per kg body weight respectively (P<0.01). Renal blood flow returned to control values 10-15 min after the injection of the drug.

Pentazocine, synthesized in 1958, is a benzomorphan derivative with potent analgesic properties. In addition, it is a partial narcotic antagonist and is unlikely to cause addiction (Harris and Pierson, 1964; May, 1966). Many papers have detailed the cardiovascular effects of pentazocine. However, there are few reports of the effects of the drug on the kidney. The present study presents data on the effect of pentazocine on renal blood flow.

MATERIALS AND METHODS
Twenty dogs (8-14 kg body weight) were studied. Anaesthesia, induced with pentobarbitone sodium 25-30 mg kg⁻¹ body weight, was maintained with 66% nitrous oxide in oxygen. Gallamine was administered to produce muscular relaxation and following endotracheal intubation respiration was controlled with a volume-cycled respirator. Ventilation was adjusted to maintain arterial PaCO₂ at 4.1 kPa (±0.4). Arterial PaCO₂ was measured every 15-30 min using a carbon dioxide electrode (Radiometer, PHM 72). A mixture of glucose 5% in water and lactated Ringer (1:1) was infused via a jugular vein at a rate of 4 ± 1 ml kg⁻¹ h⁻¹ throughout the experiment. (The rate of infusion required to maintain constant renal blood flow and urinary excretion had been defined in 10 dogs during a pilot study.) Central venous and arterial pressures were measured with strain-gauge transducers via femoral and venous arterial catheters. Aortic blood flow and renal blood flow were measured with square wave electromagnetic flowmeters (Nihon Koden ME-2), through a right-lateral thoracotomy and left-paramedian laparotomy respectively. The point of zero flow was determined at the end of the experiment. Pentazocine, diluted with physiological saline to 1 mg ml⁻¹, was given by bolus injection through a three-way stop-cock into the jugular vein catheter without alteration in the rate of the infusion. All measurements were taken at the end-expiratory point.

Experiment A
In 14 dogs the effects of the administration of pentazocine were studied 2-3 min after the injection of the drug. In this group, control values were obtained 2-3 min after the injection of 3 ml of physiological saline.

Experiment B
In six dogs the effects of the administration of pentazocine were studied for 20-30 min. In this group the baseline values obtaining before the injection of pentazocine were taken as the control values.

RESULTS

Experiment A
Two to three minutes after the injection of pentazocine 1 mg kg⁻¹ and 2 mg kg⁻¹ body weight, renal blood flow had decreased to 81% and 77% of control respectively (fig. 1). The decreases observed with both doses of pentazocine were significant (P<0.01).

Renal vascular resistance was inversely related to renal blood flow (r = -0.87; fig. 2), and as a result, was increased to 131% and 133% of control following the administration of pentazocine 1 mg kg⁻¹ and 2 mg kg⁻¹ body weight respectively (P<0.01).
Experiment B

Following the administration of pentazocine, the renal blood flow was noted to decrease transiently, the maximum change occurring 2–3 min after the injection. Renal blood flow had returned to control values 10–15 min after administration of the drug (fig. 3).

DISCUSSION

In this study it has been shown that renal blood flow decreased in a dose-dependent manner 2–3 min following the i.v. administration of pentazocine.

Renal blood flow is regulated by complex neural and humoral factors (Rosen, 1972; Barger and Herd, 1973). In human subjects Sigman and Eldwood (1967) reported a decrease in the effective renal plasma flow, and concluded that the change was a result of vasoconstriction. In the present study, renal vascular resistance and central venous pressure were increased significantly, and there was an increase, although not significant, in total peripheral resistance. These facts indicated that the change in renal blood flow was a result of vasoconstriction.

The changes observed in the other variables, 2–3 min after the injection of the two doses of pentazocine are presented in table I.
<table>
<thead>
<tr>
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<th>Pentazocine 1 mg kg⁻¹</th>
<th>Pentazocine 2 mg kg⁻¹</th>
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<tbody>
<tr>
<td></td>
<td>Control</td>
<td>After drug</td>
</tr>
<tr>
<td>Renal blood flow (ml 10 kg⁻¹ min⁻¹)</td>
<td>62.9 ± 9.5 (n = 12)</td>
<td>49.3 ± 10.2* (n = 12)</td>
</tr>
<tr>
<td>Aortic flow (ml kg⁻¹ min⁻¹)</td>
<td>107 ± 11.9 (n = 11)</td>
<td>116 ± 20.5 (n = 11)</td>
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<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>99 ± 18.6 (n = 11)</td>
<td>101 ± 22.4 (n = 11)</td>
</tr>
<tr>
<td>Total peripheral resistance (dyne s⁻¹ cm⁻⁵)</td>
<td>8981 ± 3290 (n = 10)</td>
<td>9082 ± 3284 (n = 10)</td>
</tr>
<tr>
<td>Central venous pressure (cm H₂O)</td>
<td>4.6 ± 1.3 (n = 10)</td>
<td>4.9 ± 1.6 (n = 10)</td>
</tr>
<tr>
<td>Heart rate (beat min⁻¹)</td>
<td>145 ± 30.9 (n = 11)</td>
<td>134 ± 34.1* (n = 11)</td>
</tr>
<tr>
<td>Renal vascular resistance (%)</td>
<td>131 ± 29%* (n = 11)</td>
<td>133 ± 29%* (n = 11)</td>
</tr>
</tbody>
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* Statistically significant (P < 0.01) change from the control.

**Fig. 3.** Renal blood flow changes after pentazocine. Open circles represent control dogs after physiological saline.
Following the administration of pentazocine, Coronelos and colleagues (1974) showed that there was rapid and uniform distribution of the drug in the brain. Other reports on the central neuro-humoral effects indicate that pentazocine may stimulate the vasomotor centre. It is possible that slight vasomotor centre excitation could be intensified by the renin-angiotensin system (Barajas, 1964). An increase in aldosterone concentrations in man following pentazocine–droperidol anaesthesia when compared with fentanyl–droperidol anaesthesia was reported by Ishihara and others (1974), and suggested that the plasma concentrations of renin and angiotensin were increased. Tammisto and others (1971) reported that the concentration of circulating catecholamines was increased after an i.v. injection of pentazocine. It is known that renin–angiotensin and catecholamines interact with each other and could produce a renal vascular effect (Wathen et al., 1965; Laragh and Sealey, 1973; Regoli, Park and Rioux, 1974).

It is possible also that pentazocine has a direct vasoconstrictor effect and could be the cause of the changes in renal blood flow noted in this study. Nevertheless, the present study has not defined clearly the cause of the changes in renal blood flow and further studies are indicated.

ACKNOWLEDGEMENTS

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REFERENCES


EL EFECTO QUE EJERCICE LA PENTAZOCINA SOBRE LA CIRCULACION DE SANGRE RENAL

SUMARIO

Se anestesizaron 20 perros (peso 8–14 kg) con 25 mg de pentobarbitona sódica por cada kg de peso del cuerpo y la anestesia fue mantenida con óxido nitroso en oxígeno. Se
controló la respiración con un respirador de volumen limitado \((P_{aco}, 4.7 \pm 0.4 \text{kPa})\). Se midió la circulación de sangre renal con un medidor electromagnético de circulación de onda rectangular introducido mediante una laparotomía paramediana izquierda. La circulación de sangre renal disminuyó momentáneamente tras una inyección intravenosa de pentazocina. Las disminuciones fueron de 81\% \pm 10,8 y 77\% \pm 3 de control, tras la administración de pentazocina 1 mg y 2 mg respectivamente por cada kg de peso del cuerpo \((P<0.01)\). La circulación de la sangre renal volvió a los valores de control entre 10 y 15 min después de la inyección de la droga.