Lowering of blood pressure, plasma renin substrate, cholesterol and triglyceride by portacaval anastomosis in rats fed on a 60% sucrose/5% lard diet

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Summary

1. Portacaval anastomosis was carried out in ten rats fed on a 60% sucrose/5% lard diet, which induced moderate hypertriglyceridaemia, mild hypercholesterolaemia and normotension.

2. Plasma triglyceride was decreased to 45% of concentrations observed in ten pair-weighed control rats.

3. Plasma cholesterol concentrations were reduced to 58%, renin substrate to 70% and aortic blood pressure to 80% of control values by portacaval shunt surgery.

4. Individual blood pressures were directly related to plasma renin substrate concentrations.

Key words: blood pressure, cholesterol, hyperlipidaemia, portacaval anastomosis, renin, triglyceride.

Introduction

A recent report has described regression of atherosclerosis and severe hypercholesterolaemia in a 12-year-old girl with homozygous type IIa hyperlipoproteinaemia after portacaval anastomosis (Starzl, Putnam, Chase & Porter, 1973; Starzl, Chase, Putnam, Nora, Fennell & Porter, 1974).

Methods

In the present study, twenty non-fasting white rats, paired for sex, weight and age, were fed a 60% sucrose/5% lard diet, in order to produce type IV hyperlipidaemia in control animals (Shiff, Roheim & Eder, 1971). End-to-side portacaval anastomosis (Herz, Sautter, Robert & Bircher, 1972) was performed in one of each pair of rats by one of us (K.D.G.E.); rats were given free access to the sucrose/lard diet postoperatively. Control rats were pair-fed by limiting intake of the sucrose/lard diet to match body weights throughout (pair-weighed). On this diet, contrary to previous reports (Herz et al., 1972), rats with portacaval shunt gained weight postoperatively, as did pair-weighed control rats; during the last 14 days, the mean rate of increase in body weight, from 275 g after portacaval anastomosis, was 3 g/day, and in pair-weighed control rats was 2.3 g/day.

Results

Mean non-fasting plasma total cholesterol and triglyceride concentrations were measured in rats 3 weeks postoperatively after exsanguination by aortic puncture during laparotomy under ether anaesthesia. Plasma total cholesterol and triglyceride concentrations were lowered by 42 and 55% respectively by portacaval anastomosis: mean values ±SEM were 103±5 and 170±19 mg/100 ml in pair-weighed control rats compared with 60±4 and 76±9 mg/100 ml in rats after portacaval shunt surgery. The differences were significant by paired t-test \([P<0.001]; 9 \text{ degrees of freedom (d.f.)}\]. Mean aortic blood pressure was 20% lower in rats after portacaval anastomosis than in control rats, which had an average blood pressure of 105±5 mmHg, and the difference was significant \((P<0.010)\) by paired t-test \((6 \text{ d.f.})\). Portacaval anastomosis caused a 37% reduction in hepatic weight \((2.49±0.12\% \text{ of body weight compared with } 3.92±0.11\% \text{ in pair-weighed control rats}; \ P<0.001; 9 \text{ d.f.})\) and significant 14% and 29% increases in cardiac and individual renal weights: each 0.39±0.02\% of body weight, compared with 0.34±0.01\% and 0.31±0.01\% in control rats \(P<0.001 \text{ and } <0.005 \text{ respectively};\)
Increased renal weight was associated with increased or high-normal clearances of inulin and p-aminohippurate, relative to body weight (J. B. Coelho & K. D. G. Edwards, unpublished observations). Plasma albumin concentrations were significantly decreased by 27% from 4.3 ± 0.3 g/100 ml in pair-weighed control rats to 3.1 ± 0.2 in portacaval shunt rats (P < 0.001); plasma globulin increased significantly from 2.0 ± 0.7 to 3.2 ± 0.2 g/100 ml (P < 0.001), and plasma total protein remained unchanged (9 d.f.).

A hypothesis that the blood pressure-lowering effect of PCA may be related to decreased hepatic synthesis and a fall in plasma concentration of renin substrate is supported by finding a significant (P < 0.005) 30% fall in the latter. Furthermore, the fall in blood pressure correlated significantly in direct linear fashion with the fall in plasma renin substrate concentration (P < 0.05; 8 d.f.).

**Discussion**

It is proposed that the mechanism of action of the portacaval shunt operation may depend mainly on decreased hepatic synthesis of proteins and lipids, reduced blood flow and hepatocytic shrinkage, together with hormonal changes related to portal diversion and decreased liver mass (Flynn & Kennan, 1968; Starzl et al., 1973, 1974; Bilheimer, Goldstein, Grundy & Brown, 1975). Reduction in cholesterol synthesis and low-density lipoprotein synthesis after portacaval anastomosis has recently been demonstrated together with marked increases in the plasma concentrations of bile acids and glucagon (Herz et al., 1972; Bilheimer et al., 1975). Reduced hepatic synthesis occurs without significant change in biliary excretion of bile salts derived from cholesterol catabolism (Herz, Paumgartner & Preisig, 1974) or in lipoprotein catabolism (Carew, Saik, Johansen, Dennis & Steinberg, 1974).

These findings raise the hypothetical possibility that portacaval anastomosis may lower plasma renin substrate concentrations and hence blood pressure by decreasing hepatic synthesis of renin substrate, and that this may have anti-hypertensive value when blood pressure is high. Recent studies by Schwartz and colleagues in New York strongly support this. In these studies (Schwartz, McCabe & Zintel, 1966) the operation of “portacaval transposition” (end-to-end portacaval anastomosis combined with above-kidney end-to-end cavalportal shunt) was found to reverse or prevent arterial hypertension caused by renal artery stenosis and experimental arteriolar nephrosclerosis in dogs. Both of these conditions were associated with a rise in juxtaglomerular activity, renal renin content, peripheral plasma renin activity and angiotensin concentration (Schwartz, Alpert, Sommers & Mason, 1969).

Furthermore, hypertension induced in dogs by unilateral radiation nephritis was completely prevented, or corrected after 30–40 weeks by portacaval transposition (Schwartz et al., 1969). Although plasma renin substrate and renin concentrations were not measured, the histological findings in the kidney suggested that plasma renin was still elevated, and substrate must have been depleted in order to obtain reversal of blood pressure to normal.

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**References**


