Changes in Prostanoid Synthesis in Response to Diet and Hypertension in One-Kidney, One Clip Rats

JAMES P. CODDE, HELEN M. MCGOWAN, ROBERT VANDONGEN, AND LAWRENCE J. BEILIN

SUMMARY  This study was designed to examine the effects of diets that alter prostaglandin biosynthesis on the blood pressure in one-kidney, one clip rats with established hypertension and to compare the prostanoid generating capacity of hypertensive animals with those that remained normotensive. Rats attaining blood pressures of at least 180 mm Hg within 8 weeks of nephrectomy and renal artery stenosis were paired by weight and blood pressure and then placed on either a safflower oil or a prostaglandin I₂ inhibitory diet (cod liver oil-linseed oil mix) for 4 weeks. Animals with blood pressures of less than 150 mm Hg were also paired for the same two dietary regimens. Comparison between the two blood pressure groups revealed that on both dietary regimens hypertensive rats produced significantly more aortic 6-keto-prostaglandin F₁α and serum thromboxane B₂. Rats on the cod liver oil-linseed oil diet incorporated eicosapentaenoic acid into tissue stores with a corresponding decrease in arachidonic acid and significantly impaired ability to generate serum thromboxane B₂ (36%), aortic 6-keto-prostaglandin F₁α (65%), renal homogenate 6-keto-prostaglandin F₁α (64%) and prostaglandin E₂ (58%), and urinary prostaglandin E₂ (70%) and 6-keto-prostaglandin F₁α (52%). Despite these differences in prostanoid synthesizing capacity, no differences in blood pressure were observed between the safflower oil-fed rats and rats fed cod liver oil-linseed oil within either the hypertensive or normotensive groups. These results suggest that prostanoids do not play a major role in maintaining blood pressure in established one-kidney, one clip hypertension. However, there was enhanced synthesis of aortic prostacyclin and serum thromboxane B₂ in hypertensive rats by mechanisms yet to be ascertained. (Hypertension 7: 886-892, 1985)

KEY WORDS  • prostacyclin • thromboxane • aorta • experimental hypertension

THE concept that prostaglandins (PGs) such as prostacyclin and PGE₂ play a role in blood pressure regulation by virtue of their vasodilator and natriuretic properties has received some support from studies in which dietary changes have been used to modify PG synthesis in various forms of experimental hypertension. The most convincing evidence comes from experiments in salt-loaded rats, in which blood pressure elevation can be induced by essential fatty acid-deficient diets, which diminish PG biosynthesis, whereas linoleic acid–enriched diets, designed to enhance PG formation, appear to delay the onset and severity of hypertension in Dahl salt-sensitive rats subject to salt loading. Findings in other models of experimental hypertension are less clear-cut. For example, an essential fatty acid–deficient diet was reported to reduce blood pressure in a renin-dependent model, the two-kidney, one clip (Goldblatt) hypertensive rat, although the experimental sample size was small. Although dietary linoleic acid enrichment can ameliorate the blood pressure rise in one-kidney, one clip hypertensive rats, a form of hypertension that is neither solely salt nor renin dependent, the specificity of this dietary effect for prostacyclin has been questioned, since similar blood pressure changes were seen in this model using ω-3 fatty acids, which suppress formation of PGs of the 2 (i.e., two double bonds in the PG molecule) series.

The present study was designed to clarify the role of prostacyclin in rats with established one-kidney, one clip hypertension through the use of diets with contrasting effects on the biosynthesis of the 2-series prostanoids. Because increased generation of aortic PG-like material has been reported in deoxycorticosterone acetate–salt, two-kidney, one clip, and spontaneously hypertensive rats, the experiment was also designed to establish whether or not changes occurred in rats with one-kidney, one clip Goldblatt hypertension,
when animals remaining relatively normotensive after renal artery constriction were used as controls, and if so, whether these changes were restricted to the aorta or were part of a more generalized change in tissue prostanooid metabolism.

Materials and Methods

Eighty male Sprague-Dawley rats (125–190 g) were anesthetized with sodium pentobarbital, had their right kidneys removed, and had a silver clip (0.20 mm inside diameter) placed around the left renal artery. At this stage the rats were fed a standard rat chow (Milne Stock Feed, Welshpool, Perth, Australia) and allowed free access to tap water. Systolic blood pressure was measured twice weekly by tail sphygmomanometry on rats warmed to 38 °C for 10 minutes using a pneumatic pulse transducer (Narco Biosystems Inc., Houston, TX, USA), an oscilloscope to display arterial pulsations, and a calibrated mercury column. As the change in blood pressure following renal artery constriction showed considerable variation between animals, those rats that became hypertensive (arbitrarily defined as a reading of ≥ 180 mm Hg on 3 consecutive occasions) within 8 weeks of renal artery constriction were paired by weight and blood pressure and each rat then was randomly diverted to one of two synthetic oil–enriched diets for 4 weeks. The semisynthetic diet was composed of the following elements (percent wt/wt): casein, 20; macromineral mix, 2; vitamin/trace metal, 0.75; cellulose, 7; choline chloride, 0.25; corn flour, 45; sucrose, 15; fat, 10 (supplied as either safflower oil or cod liver oil/linseed oil mix, 9:1). When unpaired rats existed they were randomly assigned to a diet, and if animals remaining relatively normotensive after ligation of the rat blood vessels, snap frozen in liquid nitrogen, homogenized in 5 ml of Krebs-Henseleit buffer, and incubated at 37 °C for 10 minutes. Ice-cold acetone (8 ml) was then added, and after centrifugation at 2000 g for 10 minutes, the aqueous acetone layer was removed and stored at −20 °C for PG analysis. Eight milliliters of chloroform/methanol (2:1) mixture was added to the remaining pellet and stored at 4 °C for subsequent fatty acid analysis of the phospholipid fraction. Five milliliters of blood was allowed to clot by incubation for 1 hour at 37 °C and then was centrifuged at 2000 g for 10 minutes, and the serum was stored at −20 °C for thromboxane B2 measurement. A further 5 ml of blood was collected into tubes containing ethylenediaminetetraacetic acid and centrifuged, and the plasma was used for determination of total fatty acid composition. A 1-cm strip of aorta was incubated in 1 ml of Krebs-Henseleit buffer for 30 minutes before being removed, blotted dry, and weighed. The incubation medium was stored at −20 °C for 6-keto-PGF1α determination. Two centimeters of aorta was stored in 2 ml of a 2:1 chloroform/methanol mixture at −20 °C until the fatty acids in the phospholipid fraction were analyzed. Urinary samples were also stored at −20 °C before PGE2 and 6-keto-PGF1α analysis.

Prostaglandin Analysis

Serum, kidney homogenates, and aorta incubation buffer were assayed for their respective PGs by radioimmunoassay.15,16 The urine required purification before assay. Tritiated PGs for recovery estimations were added to 200 µl of urine, which was acidified with hydrochloric acid to pH 4, before extraction with 2 ml of chloroform. The chloroform layer was removed and dried under vacuum at 30 °C, and the residue was dissolved in 100 µl of methanol and purified by thin-layer chromatography before radioimmunoassay for PGE2 and 6-keto-PGF1α.

Fatty Acid Analysis

The chloroform-methanol extract from kidney homogenates was filtered, dried with MgSO4, and evaporated under vacuum at 40 °C. Total phospholipids were excluded from the study.

The oil component of the feed contributed 20% of the caloric content and was either safflower oil or a 9:1 mixture of cod liver oil and linseed oil (CLO/LO). The oil mixture was used because we had previously demonstrated that it inhibited PG generation more effectively than a cod liver oil diet alone.
then isolated from crude lipid extracts by thin-layer chromatography using a solvent system of hexane, ether, acetic acid, and methanol (170:40:4:4). Phospholipids were identified on plates by comparison with authentic standards (Sigma Chemical Co., St. Louis, MO, USA), and spots were visualized with iodine vapor. Analysis of acylated fatty acids in phospholipids was done by gas-liquid chromatography of their corresponding methyl esters. Methyl esters were prepared by treating samples with 14% boron trifluoride in methanol (BDH Pharmaceuticals Ltd., London, England) at 100 °C for 30 minutes. After dilution with water, methyl esters were extracted with hexane, dried under nitrogen, and then dissolved in 25 μl of hexane for gas-liquid chromatography analysis.

The methyl esters were separated using a 2-m column packed with C18-5 on 80/100 mesh Chromosorb W (Alltech Associates) and operated isothermally at 215 °C using nitrogen carrier gas (30 ml/min). Peaks were identified by comparison with authentic standards (Sigma), heptadecanoic acid was used as an internal standard, and peak areas were calculated by integration on a Packard 437 integrating chart recorder (Packard Instruments).

Renin Analysis

Renin concentration was measured by radioimmunoassay of angiotensin I generated by incubating plasma with renin substrate (prepared from nephrectomized rats) for 1 hour at 37 °C, pH 7.4, in the presence of 3 mM disodium ethylenediaminetetraacetic acid, 3.5 mM 8-hydroxyquinoline, and 1.4 mM dimercaprol.

Statistics

Two-way analysis of variance was used to test for significant variations between the hypertensive and normotensive groups on the two dietary treatments, and differences were determined by modified t statistics. Blood pressure data were analyzed by two-way repeated measures analysis of variance. Results are expressed as means ± SEM.

Results

Weights

The different dietary regimens of safflower oil–enriched and CLO/LO-enriched feeds did not alter the relative weight gain of the rats. Final predeath weights were 429 ± 14 g and 430 ± 13 g respectively in the hypertensive group and 425 ± 22 g and 442 ± 19 g respectively in the normotensive group.

Blood Pressure

The dietary treatments did not affect the blood pressures of either the hypertensive or the normotensive rats (Figure 1). In total, five hypertensive rats died during the dietary period, two in the safflower oil–fed group and three in the group fed CLO/LO. The drop in group mean blood pressure at 3 weeks in the hypertensive group that was fed CLO/LO can be attributed to the death of one of these rats with a blood pressure of 270 mm Hg. The other rats that died had blood pressures similar to their group means. The final systolic blood pressures for the hypertensive rats were 216 ± 7 mm Hg in the safflower oil–fed group and 208 ± 10 mm Hg in the group fed CLO/LO and were 149 ± 5 mm Hg and 156 ± 5 mm Hg, respectively, for the normotensive rats in the safflower oil–fed and CLO/LO-fed groups.

Renal Fatty Acid Analysis

Rats on the two dietary regimens showed different renal phospholipid compositions. Relative to the safflower oil–fed groups, the rats fed CLO/LO had lower proportions of linoleic (85%) and arachidonic acids (63%; p < 0.001) but higher proportions of oleic (143%; p < 0.001) and eicosapentaenoic (p < 0.001) acids. No differences were observed between hypertensive and normotensive rats on the same diet (Table 2).

Aortic Phospholipid Fatty Acids

Hypertensive rats on either diet had significantly lower proportions of arachidonate (75–85%; p < 0.05) than normotensive animals on the same diet. Hypertensive safflower oil–fed rats had significantly higher proportions of linoleic acid than either their normotensive counterparts (165%; p < 0.05) or the hypertensive and normotensive rats fed CLO/LO (158%; p < 0.05). Linoleic acid contents were similar in the latter three groups. The arachidonate content was higher in safflower oil–fed animals (130–142%; p < 0.05) relative to that of the groups fed CLO/LO. Animals fed CLO/LO showed increased incorporation of oleic (117%; p < 0.05) and eicosapentaenoic (p < 0.001) acids into aortic phospholipids (Table 2).

![Figure 1. Rat blood pressures during the dietary period enriched with polyunsaturated fatty acids for the hypertensive rats fed safflower (--), hypertensive rats fed cod liver oil-linseed oil (-----), the normotensive rats fed safflower oil (-----), and the normotensive rats fed cod liver oil-linseed oil (-----). Numbers are group sample sizes.](http://hyper.ahajournals.org/)
PROSTANOID CHANGES IN GOLDBLATT HYPERTENSION/Corffe et al.

TABLE 2. Major Fatty Acid Composition (percent) of Kidney, Aorta, and Plasma Samples from One-Kidney, One Clip Hypertensive and Normotensive Rats

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diet</th>
<th>Group</th>
<th>Palmitic (16:0)*†</th>
<th>Stearic (18:0)</th>
<th>Oleic (18:1)*</th>
<th>Linoleic (18:2)*</th>
<th>Arachidonic (20:4)*</th>
<th>EPA (20:5)*</th>
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</thead>
<tbody>
<tr>
<td>Kidney‡</td>
<td>S</td>
<td>H</td>
<td>15.7±0.9</td>
<td>19.5±0.7</td>
<td>10.1±0.2</td>
<td>19.0±1.0</td>
<td>34.3±0.6</td>
<td>—</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>H</td>
<td>16.5±0.5</td>
<td>18.7±0.5</td>
<td>9.8±0.2</td>
<td>19.2±1.3</td>
<td>32.6±0.7</td>
<td>—</td>
<td>10</td>
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<tr>
<td></td>
<td>CLO/LO</td>
<td>H</td>
<td>19.0±0.6</td>
<td>19.3±0.4</td>
<td>14.3±0.2</td>
<td>16.6±1.2</td>
<td>20.3±0.8</td>
<td>8.4±1.3</td>
<td>7</td>
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<tr>
<td></td>
<td>CLO/LO</td>
<td>N</td>
<td>17.5±0.5</td>
<td>19.0±0.3</td>
<td>14.3±0.3</td>
<td>16.6±0.6</td>
<td>21.0±0.5</td>
<td>9.2±0.3</td>
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</tr>
<tr>
<td>Aorta‡</td>
<td>S</td>
<td>H</td>
<td>22.8±0.9</td>
<td>22.3±1.0</td>
<td>14.8±0.9</td>
<td>18.5±2.3</td>
<td>11.9±1.3</td>
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<tr>
<td></td>
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<td>25.9±0.8</td>
<td>24.2±0.9</td>
<td>14.3±0.7</td>
<td>11.2±1.4</td>
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<tr>
<td></td>
<td>CLO/LO</td>
<td>H</td>
<td>25.2±1.0</td>
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<td>12.8±2.5</td>
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<td>CLO/LO</td>
<td>N</td>
<td>25.2±1.1</td>
<td>22.9±1.0</td>
<td>16.7±0.7</td>
<td>10.6±1.3</td>
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<tr>
<td>Plasma§</td>
<td>S</td>
<td>H</td>
<td>17.2±0.5</td>
<td>11.9±0.4</td>
<td>7.9±0.1</td>
<td>21.1±0.5</td>
<td>39.2±1.2</td>
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<td>9</td>
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<tr>
<td></td>
<td>N</td>
<td>H</td>
<td>19.3±1.2</td>
<td>12.8±1.1</td>
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<td>15.8±1.3</td>
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<td>CLO/LO</td>
<td>N</td>
<td>24.2±1.3</td>
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<td>15.0±1.1</td>
<td>7.6±1.2</td>
<td>9</td>
</tr>
</tbody>
</table>

Results are expressed as means ± SEM.
Where differences existed between hypertensive and normotensive groups on the same diet, the hypertensive group has been italicized (p < 0.05).
EPA = eicosapentaenoic acid; S = safflower oil; H = hypertensive; N = normotensive; CLO/LO = cod liver oil–linseed oil.
* p < 0.05, differences between dietary groups. Probabilities were determined by modified r statistics after a significant two-way analysis of variance result.
† Difference not significant in aortic strip analysis.
‡ Phospholipid composition.
§ Total lipid composition.

Plasma Fatty Acids
The total lipid fraction of plasma showed no significant differences in fatty acid composition between hypertensive and normotensive animals on the same diet. Relative to the safflower oil–fed rats, the rats fed CLO/LO had higher proportions of palmitic (135%; p < 0.001), oleic (199%; p < 0.001), and eicosapentaenoic (p < 0.001) acids. These changes were accompanied by reduced proportions of linoleic (72%; p < 0.001) and arachidonic (41%; p < 0.001) acids (Table 2).

Serum Thromboxane B2 Generation
Hypertensive rats had higher levels of thromboxane B2 than did normotensive animals on the same diet (134–148%; p < 0.001). Thromboxane B2 levels generated by incubation of whole blood were significantly lower in rats fed CLO/LO than those found in the safflower oil–fed animals (34–38%; p < 0.001).

Aortic 6-Keto-Prostaglandin F1α Generation
Hypertensive rats on both dietary regimens generated substantially more 6-keto-PGF1α than the normotensive animals (188–225%; p < 0.001). Levels of 6-keto-PGF1α were lower in the rats fed CLO/LO relative to those on the safflower oil diet (59–70%; p < 0.05).

Renal Prostaglandin Generation
No differences in renal PG generation were observed between hypertensive and normotensive rats on the same diet. Rats on the CLO/LO diet showed lower renal PGE2 (54–61%; p < 0.05) and 6-keto-PGF1α (60–68%; p < 0.001) generating capacity than those on the safflower oil diet.

Urinary Prostaglandin Excretion
Urinary PG excretion followed a similar pattern to that observed in renal homogenate with the group fed CLO/LO, which showed diminished levels of PGE2 (59%; p < 0.05) and 6-keto-PGF1α (55%; p < 0.001) relative to the group fed safflower oil (Figure 2). Although PG inhibition also occurred in the normotensive group fed CLO/LO, it was only significant for 6-keto-PGF1α (51%; p < 0.001). There were no differences between the hypertensive and normotensive rats on the same diets.

Plasma Renin Activity
No significant differences in plasma renin activity were observed between the four treatment groups. Levels in the hypertensive groups fed safflower oil and CLO/LO were 2.7 ± 0.5 (ng angiotensin I generated/min) and 3.6 ± 1.1, respectively, and 4.6 ± 1.2 and 3.9 ± 0.9, respectively, in the normotensive groups fed safflower oil and CLO/LO.

Discussion
It has previously been reported that a linoleic acid–enriched diet protected against salt-induced hypertension.19 Similarly, linoleic acid supplementation delayed the onset of hypertension and prevented about
half of the ultimate rise in blood pressure in salt-loaded Dahl salt-sensitive rats, with a concomitant increase in renal PGE$_2$ synthesis. In the present study linoleate enrichment resulted in a significantly higher capacity to generate PGs in vivo and in vitro relative to eicosapentaenoate-fed animals, but group mean blood pressures were almost identical in the two oil-treated groups with established one-kidney, one clip hypertension. These results are consistent with our previous studies in which suppression of PG synthesis by feeding linolenate-enriched diet before renal artery constriction failed to elevate blood pressure over and above linoleate and standard chow-fed animals. Hoffman and Forster found that dietary linolenic acid enrichment in spontaneously hypertensive rats did not raise blood pressure but in fact lowered it relative to that found in groups fed saturated fat and sunflower seed oil (46% linoleic acid) diets. Thus, it would appear unlikely that any of the protective effect of increased dietary linoleic acid against blood pressure elevation reported in some models of experimental hypertension is mediated by increased PG synthesis rather than by nonspecific effects of increased polyunsaturated fat intake. Moreover, in rat models studied to date, dietary induced suppression of PG synthesis does not appear to accentuate hypertension, except when a diet deficient in essential fatty acids leads to an impaired ability to excrete a salt load.

In the present study, the CLO/LO diet resulted in the incorporation of eicosapentaenoic acid into renal and aortic tissues with a concomitant decrease in arachidonic acid and a diminished capacity to synthesize prostanooids relative to safflower oil-fed rats. Marine oils such as cod liver oil reduce PG synthesis mainly through the actions of two fatty acids present in high concentrations. Eicosapentaenoic and docosahexaenoic acids strongly inhibit the conversion of arachidonate to PGs by competing for binding sites on cyclooxygenase. Relative to the safflower oil-fed groups, prostanooid levels were diminished in all tissue incubates and in urine samples in the groups fed CLO/LO, which indicates both in vitro inhibition, as reported by Ziboh and Pace-Asciak and Wolfe, and in vivo suppression of renal PGE$_2$ and 6-keto-PGF$_{1\alpha}$ production (Figure 2). The degree of inhibition varied between tissues, ranging from a 64% reduction in serum to a 36% to 42% reduction in kidney to a 35% reduction in aorta to a 30 to 48% reduction in urine. It is of interest that the degree of inhibition paralleled the reduction of arachidonate levels in these tissues (i.e., plasma, 59%; kidney, 38%; and aorta, 29%). There is still some uncertainty as to whether feeding rats eicosapentaenoic acid and other fatty acids of the $\omega$-3 series leads to formation of the $\omega$-3 series prostanooids, such as PGI$_3$, which has recently been demonstrated in human urine. This question is important to resolve, since

![Figure 2. Tissue and urinary prostanooid synthesis in hypertensive (H) and normotensive (N) rats. Results shown as means and SEM. Rats fed safflower oil are indicated by open bars; rats fed cod liver oil–linseed oil are indicated by shaded bars; 6-keto-PGF$_{1\alpha}$ = 6-keto-prostaglandin F$_{1\alpha}$; PGE$_2$ = prostaglandin E$_2$; TXB$_2$ = thromboxane B$_2$; ns = not significant. Results, by two-way analysis of variance, of significant differences between dietary groups (*p < 0.05, **p < 0.001) and between hypertensive and normotensive groups (††p < 0.001).]
synthesis of the vasodilator PG12 theoretically could counterbalance any effect of suppression of PG12 and PGE2 synthesis.

Measurement of prostanooid synthesis in vitro showed that hypertensive rats generated significantly more aortic 6-keto-PGF1α and serum thromboxane B2 than their normotensive counterparts, regardless of dietary suppression of prostanooid synthesis (Figure 2). Increased aortic PG generation has been described previously in spontaneously hypertensive rats27,30 and in renal clip and deoxycorticosterone acetate–salt hypertensive rats.30 In addition, we have previously observed a correlation between aortic 6-keto-PGF1α levels and systolic blood pressure in one-kidney, one clip hypertensive rats.8,9

The question arises as to how these changes in aortic 6-keto-PGF1α in vitro relate to vascular prostacyclin synthesis in vivo. One suggestion has been that hypertrophy or cellular proliferation in vascular tissue may be responsible for an increase in PG synthetic capacity.29 Other studies have demonstrated enhanced conversion of exogenous arachidonate to PG12 by aortae of spontaneously hypertensive rats22 and renal clip hypertensive rats.30 Dusting et al.31 have suggested that these results may be explained by induction of PG cyclooxygenase in compensation for decreased availability of free endogenous arachidonate. Analysis of the aortic phospholipid fatty acid composition in the present study supports this hypothesis, as hypertensive rats on both dietary regimens had significantly lower proportions of arachidonic acid and a tendency to have more linoleic acid than normotensive rats. Thus, the higher levels of aortic 6-keto-PGF1α observed in the incubates of hypertensive rats may merely be the result of enhanced activity of the cyclooxygenase system and excessive release of arachidonic acid from phospholipid stores by physical trauma in vitro, which would represent the reverse of the in vivo situation.

These observations raise the possibility that the reason only some rats become hypertensive after renal artery constriction is because of a defect in their capacity to convert linoleic to arachidonic acid, which results in diminished biosynthesis of prostacyclin in vivo. Further support for diminished prostacyclin synthesis in hypertension comes from an experiment by Falardeau and Martinneau32 in which they used urinary 2,3-dinor-6-keto-PGF1α as a measure of in vivo PG12 biosynthesis. They observed that a high sodium intake in Dahl rats was associated with a rise in the overall production of PG12 in salt-resistant but not in salt-sensitive rats, which suggests that impairment of prostacyclin production was responsible, at least in part, for the higher blood pressure in the Dahl salt-sensitive rats.

An alternative hypothesis is that increased levels of aortic 6-keto-PGF1α in hypertensive rats reflects a vasodilator mechanism responding to elevated blood pressures.12,33 Support for this theory comes from accentuation of systemic blood pressure after administration of PG cyclooxygenase inhibitors34 and a greater hypotensive effect of intravenous arachidonate in hypertensive animals than that observed in controls.30 Further studies are needed to throw light on the mechanism of enhanced enzyme activity observed in hypertensive animals and the relation of this to in vivo prostacyclin synthesis.

The greater amounts of thromboxane B2 generated by the incubation of whole blood from hypertensive animals relative to the normotensive animals may reflect increased activity of the cyclooxygenase system in platelets. This observation is more difficult to explain as an adaptive response to blood pressure elevation, but conceivably endothelial damage associated with hypertension results in increased platelet–endothelial interactions, which may stimulate platelet cyclooxygenase activity.

No significant differences were observed between the two blood pressure groups in the amount of PGs generated by renal homogenate or excreted in urine. This result contrasts with some reports of increased renal PG synthesis in spontaneously hypertensive rats relative to that of their Wistar-Kyoto rat controls.35,36 Although a higher level of PG synthesis in the spontaneously hypertensive rat may be a response to the increased renal perfusion pressure, the sole kidney of one-kidney, one clip hypertensive rats is protected from the high systemic pressures and may even have lower intrarenal pressures than normal.30 This characteristic may account for the similar renal and urinary PG levels observed between hypertensive and normotensive rats in the present experiment.

In conclusion, dietary supplementation with linoleic acid or oils rich in eicosapentaenoic and linolenic acids caused significant changes in tissue prostanooid production in vitro, and urinary PG excretion in vivo, in one-kidney, one clip hypertensive rats without influencing blood pressures of either hypertensive or normotensive animals. Furthermore, marked differences in aortic and serum prostanooid generating capacity occurred between the hypertensive and normotensive rats irrespective of the dietary regimen.

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