Effects of Indomethacin on Renal Hemodynamic Alterations Caused by Arterial and Ureteral Pressure Changes in Rabbits

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SUMMARY

Roles of prostaglandins in renal autoregulation and the distribution of cortical blood flow were studied in anesthetized rabbits, by means of prostaglandin synthesis inhibition. Within the range from 80 to 130 mmHg in renal perfusion pressure, a constancy of renal blood flow was maintained. With an abrupt elevation of perfusion pressure from 100 to 130 mmHg, blood flow did not alter in any regions of the cortex. In contrast, when perfusion pressure was reduced from 100 to 80 mmHg, blood flow decreased in the outer cortex with reciprocal increase in the inner cortex. These hemodynamic changes were not affected by indomethacin. Acute ureteral pressure elevation to 50 mmHg resulted in a redistribution of cortical flow to the inner cortex without significant change in renal blood flow. This redistribution was inhibited by indomethacin. During ureteral pressure elevation, autoregulation was impaired. In this situation, a rise of perfusion pressure produced a significant increase in blood flow in the outer cortex without significant change elsewhere. A reduction of perfusion pressure gave rise to significant decrease in flow in the outer cortex without an increase in the inner cortex. In indomethacin-treated rabbits, ureteral pressure elevation impaired autoregulation slightly but not significantly. These findings suggest 1) good autoregulatory capability in all regions of the renal cortex; and 2) a minor role of prostaglandins in the development of renal autoregulation in normal rabbits but a partial contribution to the impairment of autoregulation during ureteral pressure elevation.

Additional Indexing Words:
Autoregulation Ureteral pressure elevation Radioactive microsphere technique Indomethacin

There seems to exist a controversy as to the autoregulatory mechanisms in the kidney.1–3) Recent studies4) suggested that intramedullary prostaglandin synthesis was involved in renal autoregulation. Other inves-
tigators failed to confirm this hypothesis. On the other hand, renal autoregulation is impaired by ureteral pressure elevation. In addition, ureteral pressure elevation causes an increase in renal blood flow with a redistribution of flow to the inner cortex. Some investigators demonstrated that prostaglandins mediated these hemodynamic alterations. However, less information is available as to the role of prostaglandins in the impairment of autoregulation during ureteral pressure elevation.

Also, opinions are still divided as to the autoregulatory capability in different layers of the renal cortex. Thurau et al. found poor autoregulation in the inner medulla of dogs, using the photometric method. Other investigators have demonstrated more or less complete autoregulation in all regions of the renal cortex of dogs, cats, and rats, utilizing the inert gas clearance technique, ferrocyanide method or micropuncture technique. In apparent disagreement with these findings, the microsphere distribution indicated that reduction of renal perfusion pressure resulted in a decrease in blood flow in the outer cortex with reciprocal increase in the inner cortex.

The present experiments were attempted to reexamine roles of prostaglandins in renal autoregulation and the autoregulatory capability in various layers of the renal cortex in rabbits. The results suggest 1) good autoregulatory capability in all regions of the renal cortex; and 2) a minor role of prostaglandins in the development of renal autoregulation in normal rabbits but a partial contribution to the impairment of autoregulation during ureteral pressure elevation.

**Methods**

Experiments were carried out in 50 rabbits, weighing between 2.8 and 3.2 Kg and allowed free access to commercial rabbit chow and drinking water. The animals were anesthetized with intravenous sodium pentobarbital (30-35 mg/Kg of body weight) and subsequently given small maintenance doses as necessary. The left kidney was exposed through a midabdominal incision. The kidney vessels were cleared of all surrounding tissues. In order to examine the ability of kidney to autoregulate blood flow, arterial blood pressure was rapidly elevated from the control value of approximately 100 to 130 mmHg by bilateral carotid occlusion with clamps or reduced to 80 and 60 mmHg by constricting the aorta with an adjustable clamp. A minimum of 10 min was allowed between successive occlusions. Pressure and flow measurements were made before and 3 min after changing perfusion pressure. During the experiment isotonic saline solution was intravenously infused at a constant rate (0.3 ml/min) to replace loss of body fluid.

Instead of renal perfusion pressure, aortic pressure was measured just below the origin of the left renal artery with a Statham pressure transducer (P23AA) connected to a catheter inserted into the abdominal aorta through the right femoral artery. Renal blood flow was measured by a square-wave electromagnetic flow-
meter (ME-5, Nihon Koden Co, Japan). A flow probe of 1.5 mm ID (MF-2T, Nihon Koden Co) was placed on the renal artery. The zero-flow base line was determined by a brief occlusion of the artery distal to the probe. At the completion of the experiment, the probe mounted on the isolated renal artery was calibrated with rabbit's blood. The efficiency ratios of autoregulation (AER) were calculated from the formula of Semple and de Wardener. A ratio of zero indicates perfect autoregulation, and a ratio of one indicates absence of autoregulation.

Regional blood flows in the different layers of the renal cortex were estimated by the radioactive microsphere technique described by McNay and Abe as previously reported. The nuclides used were strontium 85 and cerium 141 (3M Co, St Paul, Minn). Approximately 220,000 microspheres, 15 ± 5 μm in diameter, were given. The nuclide to be given was suspended in 1 ml of 20% dextran solution, injected through a catheter introduced into the left ventricle, and then flushed with heparinized saline solution. The first microsphere injection was given 3 min before changing perfusion pressure. The second injection was performed 2 min after a stable blood flow had been established during perfusion pressure elevation or reduction. The microsphere injection did not significantly affect renal hemodynamics. At the conclusion of the experiment the kidney was removed, weighed, measured in 3 dimensions, and middle triangular renal tissue blocks, containing the cortex and medulla, were quick-frozen in a dry ice-acetone mixture. Cortex thickness was measured. While still frozen the cortex was separated from the medulla with a razor blade and divided into 4 equal zones, which were to be called zone C-1 through C-4, from the outer cortex inward. Each cortical tissue slice was weighed, and its radioactivity was counted in a well scintillation counter. Strontium 85 and cerium 141 were counted at the 0.514 and 0.145 meV peaks, respectively. No correction was necessary for the 85Sr counts, but the true 141Ce counts were estimated as

$$\text{true } 141\text{Ce counts} = C - S \cdot B / A$$

where C, S, B, and A were the radioactivity of the tissue slice measured at the 0.145 and 0.514 meV peaks, and the counts of a standard 85Sr sample estimated at the 0.145 and 0.514 meV peaks, respectively. Histological observations revealed that most of microspheres, which entered the kidney, were trapped in the glomerular capillaries. Radioactivity in the medullary tissue averaged 1.7 ± 0.57% of the count of total kidney. Radioactivity in venous blood was negligible. McNay and Abe's study suggests that axial migration of microspheres does not occur in the interlobular arteries. Therefore, the quantity of the nuclides per unit of tissue weight in each cortical layer is a function of regional glomerular capillary flow. The percentage of total blood flow perfusing each cortical layer was calculated as

$$\text{percentage flow} = \left( \frac{C_i \cdot W_i}{\sum C_i \cdot W_i} \right) \times 100\% \quad (i = \text{zones } 1-4)$$

where C was the radioactivity per unit tissue weight in each cortical layer, W was total weight of the zone, and \( \sum C_i \cdot W_i \) the radioactivity per total renal cortex. The weight of each cortical layer was approximated by calculations based on the formula for an ellipsoid. A series of volumes were calculated by sequential reductions in each hemiasxis by an amount equal to one-fourth of the cortex thickness. Absolute blood flow rate in the cortical layers, presented as milliliters per minute per gram of tissue weight, was calculated on the basis of total renal blood
Also, regional vascular resistance was calculated from the values of abdominal aortic pressure and regional blood flow.

Also studied was the effect on the intrarenal hemodynamics of indomethacin, a prostaglandin synthetase inhibitor, to determine whether a prostaglandin mechanism contributed to circulatory autoregulation and cortical flow distribution. Indomethacin, 5 mg/Kg of body weight, a dose well above that needed to inhibit prostaglandin synthesis in dogs and rabbits,\textsuperscript{26,27} was intravenously injected. The drug was dissolved in a 0.67\% sodium carbonate solution.\textsuperscript{24} The diluent had no significant effect on arterial pressure, renal blood flow and the distribution of cortical flow.\textsuperscript{24} After indomethacin was given, a minimum of 20 min was required for renal blood flow and pressure to stabilize.\textsuperscript{24} The effect of indomethacin on circulatory autoregulation was examined between 30 and 60 min after the injection.

In order to examine the effects of ureteral pressure elevation on autoregulatory capability and the distribution of cortical blood flow, the pressure to flow relationship were evaluated during ureteral pressure elevation in normal and indomethacin-treated animals. The left ureter was cannulated with a polyethylene tube connected to a pressure bottle, and ureteral pressure was raised to approximately 50 mmHg.

For statistical analysis Student's t-test was used. All data are presented as mean±SE.

**RESULTS**

*Cortical blood flow distribution during autoregulatory adjustments:*

The effect of an abrupt elevation of renal perfusion pressure on the distribution of blood flow was studied in the renal cortex of 6 rabbits. When arterial pressure was acutely raised from 103±5.2 to 126±8.1 mmHg, total renal blood flow was not altered from the control value of 31.4±4.95 ml/min, exhibiting an excellent autoregulation (AER -0.03±0.098) (Table I). Also, the fractional and absolute blood flows did not significantly change in each cortical layer.

In another 5 animals a reduction in perfusion pressure from the control level of 99±1.9 to 81±2.4 mmHg was associated with an insignificant decrease in renal blood flow from 33.9±4.44 to 33.4±4.40 ml/min (AER 0.07±0.053) (Table I). In contrast to the findings obtained during perfusion pressure elevation, the fractional and absolute blood flows decreased in the outer cortex C-1 with reciprocal increases in the inner cortices C-3 and C-4 (p<0.005 and p<0.01). In addition, a reduction of perfusion pressure to 60 mmHg produced a further increase in the inner cortical flow and a further decrease in the outer cortical flow (Fig. 1 top).

*Effect of indomethacin on autoregulation:*

In 6 rabbits the autoregulatory ability was examined before and after the indomethacin administration. Prior to the administration, renal blood
Table I. Circulatory Autoregulation and the Distribution of Cortical Blood Flow in Normal Rabbits

<table>
<thead>
<tr>
<th>AP (mmHg)</th>
<th>RBF (ml/min)</th>
<th>Percent flow</th>
<th>Absolute blood flow (ml/min Gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C-1</td>
<td>C-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>103</td>
<td>31.4</td>
<td>47.1</td>
<td>23.6</td>
</tr>
<tr>
<td>±5.2</td>
<td>±4.95</td>
<td>±3.78</td>
<td>±1.36</td>
</tr>
<tr>
<td>126</td>
<td>31.6</td>
<td>47.5</td>
<td>22.4</td>
</tr>
<tr>
<td>±8.1</td>
<td>±5.69</td>
<td>±3.45</td>
<td>±1.18</td>
</tr>
<tr>
<td>p value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Perfusion pressure elevation (n, 6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td>33.9</td>
<td>45.5</td>
<td>24.8</td>
</tr>
<tr>
<td>±1.9</td>
<td>±4.44</td>
<td>±2.90</td>
<td>±2.07</td>
</tr>
<tr>
<td>81</td>
<td>33.4</td>
<td>37.8</td>
<td>25.8</td>
</tr>
<tr>
<td>±2.4</td>
<td>±4.40</td>
<td>±3.33</td>
<td>±1.37</td>
</tr>
<tr>
<td>p value</td>
<td>NS</td>
<td>&lt;0.005</td>
<td>NS</td>
</tr>
</tbody>
</table>

AP = renal perfusion pressure; RBF = renal blood flow; n = number of animals; NS = not statistically significant.

Fig. 1. The pressure to flow relationships at the levels of ureteral pressure of zero (top) and 50 mmHg (bottom). UP = ureteral pressure; AP = renal perfusion pressure; %F = the percent change of renal blood flow; TRBF = total renal blood flow.
Renal hemodynamic alterations during perfusion pressure reduction in indomethacin-treated rabbits. Open bars represent perfusion pressure (AP), renal blood flow (RBF), cortical fractional flow and absolute blood flow in different cortical layers (C-1~C-4) before perfusion pressure reduction. Hatched bars represent the data during acute perfusion pressure reduction.

Flow changed from the control value of 34.7±1.17 to 38.0±1.24 ml/min as perfusion pressure was elevated from 104±4.3 to 132±6.0 mmHg. Thirty to 60 min after the injection, renal blood flow changed from 30.8±1.78 to 34.0±3.42 ml/min in response to perfusion pressure elevation from 111±5.2 to 139±2.7 mmHg. The efficiency ratios of autoregulation were 0.39±0.060 and 0.33±0.107 before and after the injection of indomethacin, respectively, demonstrating a minor effect of indomethacin.

In another 5 indomethacin-treated animals, the effect on the cortical flow distribution of a reduction in perfusion pressure was examined. When arterial pressure was reduced from the initial level of 108±5.6 to 80±2.5 mmHg, renal blood flow did not significantly change (AER 0.20±0.114) (Fig. 2). The fractional and absolute blood flows decreased in the outer cortex C-1 (p<0.01 and p<0.05) with reciprocal increase in C-4 (p<0.05 and p<0.01) (Fig. 2). These findings are similar to the data obtained in normal rabbits.

Effects of indomethacin on renal hemodynamics during ureteral pressure elevation:

The effect of ureteral pressure elevation on the distribution of cortical blood flow was studied in 5 normal and 6 indomethacin-treated animals. When ureteral pressure was raised to approximately 45 mmHg in normal rabbits, the fractional and absolute blood flows decreased in the outer cortex (p<0.01 and p<0.05) but increased in C-4 (p<0.025 and p<0.05) without significant change in total renal blood flow (Table II). In contrast, in indomethacin-treated animals renal blood flow was significantly reduced from 39.5±4.23 to 28.9±4.21 ml/min by ureteral pressure elevation (p<0.025) (Fig. 3). The fractional blood flow increased in the outer cortex C-1 with
Table II. Effect of Ureteral Pressure Elevation on the Distribution of Cortical Blood Flow in Normal Rabbits

<table>
<thead>
<tr>
<th>AP (mmHg)</th>
<th>RBF (ml/min)</th>
<th>UP (mmHg)</th>
<th>Percent flow</th>
<th>Absolute blood flow (ml/min Gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>C-1</td>
<td>C-2</td>
</tr>
<tr>
<td>96 ± 1.8</td>
<td>28.9 ± 3.11</td>
<td>0</td>
<td>47.4 ± 2.73</td>
<td>23.8 ± 1.29</td>
</tr>
<tr>
<td>99 ± 3.3</td>
<td>28.3 ± 1.79</td>
<td>45</td>
<td>39.5 ± 3.15</td>
<td>19.8 ± 2.27</td>
</tr>
<tr>
<td>p value</td>
<td>NS</td>
<td></td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
</tbody>
</table>

Fig. 3. Effects on renal hemodynamics of ureteral pressure elevation to 50 mmHg in indomethacin-treated rabbits.

reciprocal decreases in C-2 and C-3.

In another 11 normal and 6 indomethacin-treated rabbits, the effect of ureteral pressure elevation on the autoregulatory ability of the kidney was examined. Before raising ureteral pressure, renal blood flow changed from the control value of 33.7 ± 1.51 to 37.6 ± 1.21 ml/min in 5 normal rabbits as perfusion pressure was elevated from 99 ± 3.5 to 132 ± 5.9 mmHg (AER 0.33 ± 0.048). During ureteral pressure elevation to approximately 50 mmHg, renal blood flow increased from the initial value of 34.8 ± 2.78 to 41.8 ± 2.60 ml/min in response to perfusion pressure elevation from 100 ± 2.6 to 133 ± 4.1 mmHg (AER 0.61 ± 0.09), demonstrating deterioration of the autoregulatory capability (Fig. 1, bottom and Fig. 4, top). The fractional and absolute blood flows increased in the outer cortex C-1 (p<0.05 and p<0.005) without significant change elsewhere. In 6 normal rabbits the effect of reduced perfusion pressure on the distribution of cortical flow was examined during ureteral pressure elevation (Figs. 1 and 4, bottom). Before elevating ureteral pressure, renal blood flow changed from the control value of 32.2 ± 4.59 to 30.7 ± 4.00 ml/min with an abrupt reduction of perfusion pressure from 105 ± 1.2 to 85 ± 2.1 mmHg (AER 0.26 ± 0.05). During ureteral pressure elevation to ap-
Fig. 4. Effects on renal hemodynamics of acute perfusion pressure elevation (top) or reduction (bottom) during ureteral pressure elevation (50 mmHg) in normal rabbits. Open and hatched bars indicate the data before and after changing perfusion pressure, respectively.

Approximately 48 mmHg, renal blood flow decreased from 29.8 ± 3.17 to 25.7 ± 2.97 ml/min in response to a reduction of perfusion pressure from 104 ± 2.2 to 82 ± 1.4 mmHg (AER 0.63 ± 0.145), demonstrating poor autoregulation. The fractional blood flow decreased in the outer cortex C-1 with slight increases in C-2 through C-4 (p < 0.05 and p < 0.005). The absolute perfusion rate decreased in C-1 (p < 0.005) without significant change elsewhere. A reduction of perfusion pressure to 60 mmHg resulted in significant decrease in blood flow in all cortical layers (Fig. 1, bottom). In 6 indomethacin-treated animals exhibiting the efficiency ratios of autoregulation of 0.51 ± 0.09 before ureteral pressure elevation, perfusion pressure elevation from 100 ± 1.2 to 125 ± 2.5 mmHg induced an increase in renal blood flow from 21.0 ± 1.6 to 24.0 ± 1.8 ml/min during ureteral pressure elevation to 50 mmHg (AER 0.57 ± 0.09). The difference in the efficiency ratios of autoregulation before and after ureteral pressure elevation was below statistical significance.
DISCUSSION

There seems to exist a considerable controversy as to the autoregulatory capability in the different layers of renal cortex. In the cat kidney direct measurement of hilar and capsular venous blood flows indicated equally good autoregulation in the outer and inner cortices, in agreement with the results obtained in dogs using the inert gas clearance technique. Furthermore, excellent autoregulation in glomerular filtration rate and plasma flow has been demonstrated by the ferrocyanide method and micropuncture technique in the superficial and deep glomeruli in rats and dogs. In contrast, Thurau and his coworkers found absent or poor autoregulation in the inner medulla of dogs, utilizing the photometric method. In addition, they described that blood flow in the inner medulla represented a small fraction, approximately 1%, of total renal blood flow. Medullary vasa recta are derived from efferent arterioles of juxtamedullary glomeruli which also supply the outer medullary capillary network. Juxtamedullary glomeruli have 2 efferent arterioles, one breaking into an adjacent capillary network and the other passing into the medulla as vasa recta. Therefore, it is likely that the medullary hemodynamic alterations do not always reflect those in the juxtamedullary glomeruli.

Also, recent microsphere studies have questioned the autoregulation in the superficial glomeruli. Microsphere distribution indicated that a reduction of renal perfusion pressure caused a decrease in blood flow through outer cortical glomeruli with reciprocal increase in inner cortical glomeruli. Unfortunately, in these experiments the effect of perfusion pressure elevation on the cortical flow distribution was not examined. In the present experiments, the fractional and absolute blood flows did not significantly change in any regions of the cortex as perfusion pressure was abruptly elevated, demonstrating excellent autoregulation in all regions. In response to a reduction in perfusion pressure from approximately 100 to 80 mmHg, blood flow increased in the inner cortex with reciprocal decrease in the outer cortex, supporting the findings by some investigators. However, one might hesitate to accept that an increase in blood flow could result from a reduction of perfusion pressure. The following mechanisms may be proposed to account for the paradoxical increment of blood flow: 1) increased prostaglandin synthesis in the renal medulla, 2) regional differences in renin release in the renal cortex, 3) differences in intrinsic myogenic tone of the renal vasculature in different layers of the cortex, and 4) a methodological artifact.

Stein and his coworkers have demonstrated a redistribution of blood flow toward deep nephrons and increased blood flow in the inner cortex during
renal vasodilation caused by vasodilator substances. On the other hand, a reduction in renal arterial pressure increases venous prostaglandin concentration. Prostaglandins of E series have strong vasodilator effect. However, release of prostaglandins seems to contribute little to the paradoxically increased blood flow in the inner cortex caused by perfusion pressure reduction, because of failure to abolish the redistribution of cortical flow by indomethacin, prostaglandin synthetase inhibitor.

Since renin is located predominantly in the outer cortical nephrons, a reduction of renal perfusion pressure may stimulate the local release of renin and lead to a preferential decrease in the fractional distribution of blood flow in these nephrons. In the present experiments, vascular resistance in the outer cortex C-1 did not significantly change from the control value of 11.9 mmHg/ml min\(^{-1}\) Gm\(^{-1}\) as perfusion pressure was reduced from approximately 100 to 80 mmHg (Table I), suggesting the absence of vasoconstriction through the renin-angiotensin system. Therefore, it is unlikely that the local release of renin would give rise to the redistribution of cortical flow during perfusion pressure reduction.

The third explanation is that the redistribution of cortical flow caused by hypotension, might have been due to differences in the myogenic tone of blood vessels in different layers of the cortex. Active myogenic response of the arteriole to perfusion pressure may be different in various cortical layers. The arteriole in the outer cortex may dilate maximally at normal perfusion pressure but may not in the deep cortex. This speculation seems to be supported by the data that vascular resistance in the outer cortex C-1 was relatively fixed at the level of 11.9 mmHg/ml min\(^{-1}\) Gm\(^{-1}\), whereas the resistance in the inner cortex C-4 was lowered from 29.1 to 19.3 mmHg/ml min\(^{-1}\) Gm\(^{-1}\), when perfusion pressure was reduced from approximately 100 to 80 mmHg (Table I). If this speculation is correct, it is possible that a reduction in perfusion pressure results in the redistribution of cortical flow toward the inner nephrons. However, the paradoxical increase in absolute blood flow in the inner cortex, caused by hypotension, cannot be completely explained only by this mechanism.

McNay and Abe noted that there was no significant difference between intracortical zonal flows measured by the microspheres of 36 and 18 \(\mu\)m in diameter and suggested that axial migration of microspheres did not occur in the interlobular arteries. Also, Chenitz and his coworkers have described that all microspheres smaller than 18 \(\mu\)m in diameter reach the glomerulus in rats and dogs, suggesting that in both species afferent arterioles smaller than 18 \(\mu\)m are uncommon. In contrast, Mörkrid et al have demonstrated a significant redistribution of microspheres larger than 15 \(\mu\)m from the outer
to the inner cortex during a reduction of perfusion pressure in dogs, with insignificant redistribution of smaller spheres. Also, they suggested that the redistribution of cortical flow during hypotension, estimated by the microsphere technique, was due to a methodological artifact. In the present experiments the microspheres of 15±5 μm in diameter were used. Histological examinations revealed that most of microspheres, which entered the kidney, were trapped in glomerular capillaries. If axial streaming occurs in the interlobular artery, an elevation of perfusion pressure may result in a redistribution of microspheres to the outer cortex. However, the present experiments indicated no significant redistribution of microspheres during perfusion pressure elevation. Thus, the redistribution of spheres, seen during hypotension, cannot be explained only by a methodological artifact.

The mechanism of renal autoregulation remains a subject of controversy.1)-3) Recently, intramedullary prostaglandin synthesis has been suggested to be involved in renal autoregulation.4) This hypothesis is supported by the observation that the inhibition of prostaglandin synthesis by indomethacin abolished or impaired autoregulation. In contrast, other investigators5)-8) failed to confirm this finding. Also, in the present experiments the intravenous injection of indomethacin did not significantly affect the autoregulatory capability. The reason of the discrepancy in these findings remains uncertain. Unfortunately, in this experiment the change in prostaglandin synthesis in the kidney after indomethacin was given has not been evaluated. Therefore, a question may be raised concerning the adequacy of prostaglandin synthetase inhibition by indomethacin. However, intravenous dose of 5 mg/Kg used in this work is dosage well above that needed to inhibit prostaglandin synthesis in the kidneys of dogs and rabbits.26),27) Also, this dose gave rise to a moderate decrease in renal blood flow in the face of slightly elevated systemic pressure, suggesting an inhibition of prostaglandin synthesis.24)

Some investigators9),10),31)-33) have demonstrated an increase in renal blood flow and the redistribution of flow from the outer to the inner cortex during a rise of ureteral pressure. This increase in renal blood flow has been explained by the Bayliss mechanism,24) i.e., active dilation of afferent arteriole in response to a reduction in transmural pressure caused by ureteral pressure elevation. However, recent studies31) demonstrated that prostaglandins mediated the above-described renal hemodynamic changes caused by ureteral pressure elevation. In the present experiments, a rise of ureteral pressure to approximately 45 mmHg resulted in no significant change in renal blood flow, in good accordance with previous findings33) from this laboratory that a moderate elevation of ureteral pressure resulted in an increase in renal blood flow while at higher levels above 40 mmHg the flow was reduced, probably
due to the preponderance of an increase in venous segment resistance as compared with a decrease in the prevenous segment resistance. During ureteral pressure elevation, blood flow redistributed from the outer to the inner cortex, supporting the finding by Abe and his coworkers. These hemodynamic alterations were inhibited by indomethacin administration, suggesting a contribution of prostaglandin synthesis.

During ureteral pressure elevation renal autoregulation is abolished or impaired. On the other hand, intrarenal prostaglandin synthesis is enhanced by ureteral pressure elevation. In the present experiments, acute ureteral pressure elevation deteriorated the autoregulatory ability in normal rabbits. Especially in the outer cortex, the blood flow changed in parallel fashion with perfusion pressure, exhibiting absence of autoregulation. Also, the paradoxical increase in blood flow in the deep cortex, seen during perfusion pressure reduction, was lessened during ureteral pressure elevation. However, in indomethacin-treated rabbits renal autoregulation was impaired slightly but not significantly by ureteral pressure elevation. The findings suggest that prostaglandins contribute, at least in part, to the impairment of autoregulation during ureteral pressure elevation. Enhanced prostaglandin synthesis may dilate the renal blood vessels with resultant reduced vascular tone during ureteral pressure elevation, and thus, the autoregulatory ability may be impaired.

Acknowledgments

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References


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