The Hypotensive Mechanism of Percutaneous Transluminal Dilatation (PTD) in Renovascular Hypertension Due to Bilateral Renal Artery Stenosis

SHUICHI Sasaki, YUTAKA IMAI, KEISHI ABE, MINORU NIHEI, NAOYOSHI MINAMI, MASANORI MUNAKATA, HISAO SASAKI,* HIROSHI SEKINO† and KAORU YOSHINAGA

The Second Department of Internal Medicine, *the Second Department of Surgery, Tohoku University School of Medicine, Sendai 980 and †Artificial Kidney Center, Kojin-kai Central Hospital, Sendai 980

Sasaki, S., Imai, Y., Abe, K., Nihei, M., Minami, N., Munakata, M., Sasaki, H., Sekino, H. and Yoshinaga, K. The Hypotensive Mechanism of Percutaneous Transluminal Dilatation (PTD) in Renovascular Hypertension Due to Bilateral Renal Artery Stenosis. Tohoku J. exp. Med., 1988, 154 (2), 173-183 — The hypotensive mechanism of percutaneous transluminal dilatation (PTD) in renovascular hypertension due to bilateral renal artery was investigated in two patients. Blood pressure was monitored continuously before, during and after PTD by use of a new automated blood pressure monitoring device based on finger volume-oscillometry. Plasma renin activity was measured repeatedly before, during and after PTD. A hypotensive effect appeared immediately after PTD and blood pressure remained low in the following observation period without any hypotensive medication. In these cases, the hypotension was accompanied by a transient decrease in heart rate immediately after PTD. The hypotensive response to PTD was not parallel to the basal plasma renin activity, suggesting that the renin-angiotensin system is not necessarily involved in the maintenance of the hypertension before PTD. The autonomic nervous system seemed to play a certain role. Since the hypotension was accompanied by a transient decrease in heart rate immediately after PTD, the hypotension may be induced either by a decrease in sympathetic tone or by an increase in vagal tone at least just after PTD. It is hypothesized that these changes in autonomic nervous activity are mediated centrally through the renal afferent mechanism in response to rapid changes in renal hemodynamics induced by PTD. —— percutaneous transluminal dilatation; renin-angiotensin system; autonomic nervous system; renovascular hypertension

It has been repeatedly confirmed that the percutaneous transluminal dilatation (PTD) is effective in the treatment of renal artery stenosis (Grim et al. 1981; Mahler et al. 1982; Kuhlmann et al. 1985; Millan et al. 1985). Recently PTD is recommended as a treatment of the first choice for all patients with renovascular
hypertension (RVH). However, there has been no definite explanation regarding the recovery of blood pressure (BP) to the normal range after dilatation of the renal artery stenosis in patients or experimental animals with RVH. Withdrawal of the augmented activity of the renin-angiotensin system does not always account for the depressor mechanism, since a depressor effect is obtained even in patients with normal plasma renin activity (PRA) (Marks et al. 1977; Kuhlmann et al. 1985). There are some pieces of evidence indicating that the renin-angiotensin system plays a primary role in chronic RVH (Davis 1977). However, there is also an increasing body of evidence which suggests that neural and humoral mechanisms other than the renin-angiotensin system are involved in development and maintenance of hypertension due to renal artery constriction in experimental animals (Brunner et al. 1971; Carretero et al. 1974; Keiser et al. 1976; Pamnani et al. 1976; Davis 1977). It is conceivable that the depressor effect of PTD is caused by an attenuation of some pressor mechanisms or by an activation of some depressor mechanisms. It has been reported that a depressor effect occurred within a few hours after PTD in most cases with RVH (Mahler et al. 1982; Millan et al. 1985). However, there has been no report on the detailed time course study on BP changes immediately after the PTD.

In the present study, we examined the depressor effect of PTD in patients with RVH using a new automated device for monitoring long-term BP (Yamakoshi et al. 1982a, b; Imai et al. 1986). With this device the time course of BP changes before, during and after PTD can be monitored in detail for a long period. Using this device we found that the decrease in BP was associated with a transient decrease in heart rate (HR) immediately after PTD. It may be concluded that the depressor effect just after PTD is in part induced by a change in the function of the autonomic nervous system.

**METHOD**

*Outline of the device*

The device used in the present study can automatically monitor systolic (SBP) and mean BP (MBP) in a human finger by a volume-oscillometric method. Diastolic BP (DBP) is also available. The theoretical basis of this method and technical details of this instrument have been described elsewhere (Yamakoshi et al. 1982a, b; Imai et al. 1986). Briefly, the method is designed to measure BP by detecting the local arterial volume pulsation with a photo-electric plethysmograph which is placed just below the occluding cuff. During the gradual increase or decrease in the cuff pressure, the photo-plethysmographic pulsations characteristically change in amplitude and the systolic endpoint and the point showing the maximum amplitude can be clearly discriminated. It has been confirmed that the cuff pressure values corresponding to the systolic end-point and the maximum amplitude are in good accordance with SBP and MBP in the arterial segment concerned (Yamakoshi et al. 1982a, b). Performance of the device and stability for long term BP monitoring have been reported elsewhere (Imai et al. 1986).

*Study design*

In the present study, we monitored BP and HR every 5 min in 2 patients with RVH.
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before, during and after PTD. The characteristics of these patients are shown in Table 1. In these 2 cases bilateral renal arteries stenosed more than 90%. PTD was done bilaterally in succession in one operation. Renal vein blood was taken for measuring PRA during the treatment with captopril in both cases. Both patients had been treated also by nifedipine-retard tablets. The final dose of nifedipine-retard tablet was administered 12 hr before PTD. In Case 1, the final dose of captopril was administered 2 hr before PTD. In Case 2, captopril was withdrawn a week before PTD. All studies were done in a ward setting. Plasma renin activity (PRA) was measured radioimmunologically (Abe et al. 1972). Both cases were pretreated with atropine administered intramuscularly (i.m. 0.5 mg) about an hour before PTD.

Statistical analysis was performed according to Welch-t-test, and p values (<0.01) were taken to indicate statistical significance.

RESULTS

As shown in Table 1, basal arterial pressure was high in both cases. Since atropine (0.5 mg, i.m.) was injected before PTD, tachycardia was documented during PTD. Basal PRA was abnormally high and the hyperresponsiveness of PRA to captopril (50 mg, orally) was observed in Case 1, while in Case 2 basal PRA was within the normal range and no exaggerated response to captopril (50 mg, orally) was observed. The renal vein renin ratio (right/left side) was 1.5 in the former and 1.1 in the latter.

The bilateral PTD was successfully performed in both cases (e.g. Fig. 1). Though PTD of one side of the artery scarcely changed BP, PTD of the other side

<table>
<thead>
<tr>
<th>Table 1. Blood pressure, PRA and treatment of patients with renovascular hypertension due to fibromuscular dysplasia</th>
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<tbody>
<tr>
<td>Case 1 (female, 22 years old)</td>
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<tr>
<td>Case 2 (female, 23 years old)</td>
</tr>
<tr>
<td>SBP/DBP (mmHg) averaged for 24 hr</td>
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<tr>
<td>Preceding day</td>
</tr>
<tr>
<td>153±12.2                                              154±16.1/</td>
</tr>
<tr>
<td>103±11.6                                               89±13.7</td>
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<tr>
<td>Day of PTD</td>
</tr>
<tr>
<td>128±14.6**                                           123±16.2**</td>
</tr>
<tr>
<td>89±12.4**                                             83±14.6**</td>
</tr>
<tr>
<td>Day after PTD</td>
</tr>
<tr>
<td>146±12.5**/                                           130±14.5**/</td>
</tr>
<tr>
<td>96±12.5**                                              78±9**</td>
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<tr>
<td>PRA (ng/ml/6 hr)</td>
</tr>
<tr>
<td>Before PTD</td>
</tr>
<tr>
<td>52.8                                                      6.4</td>
</tr>
<tr>
<td>24 hr after PTD</td>
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<tr>
<td>17.8                                                      15.6</td>
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<tr>
<td>48 hr after PTD</td>
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<tr>
<td>18.0                                                      12.4</td>
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<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Before PTD</td>
</tr>
<tr>
<td>Nifedipine retard tablet (20 mg t.i.d) and captopril (12.5 mg/t.i.d)</td>
</tr>
<tr>
<td>After PTD</td>
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<tr>
<td>Free                                                       Free</td>
</tr>
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</table>

Values are given in terms of mean±s.d. **p<0.01 against values on the preceding day. (Welch-t-test). PRA before PTD in Case 1 was obtained without captopril when she was admitted to the hospital. PRA, plasma renin activity.
decreased BP immediately. BP remained low during the monitoring (Table 1 and Fig. 2). A few days after PTD 24 hr BP monitoring demonstrated that BP remained low without antihypertensive medication (Fig. 3).

Fig. 4 demonstrates changes in BP and HR just after PTD. In Case 1, PTD induced a rapid hypotension which was accompanied by a decrease in HR. In Case 2, BP decreased just after PTD but the hypotensive effect was more gradual than in Case 1. A transient decrease in HR was also documented in Case 2.

**DISCUSSION**

In the present study, PTD is demonstrated to induce a rapid decrease in BP accompanied by a transient decrease in HR in patients with bilateral renal artery stenosis. Though the depressor effect of PTD has been reported to appear within
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Fig. 2. Changes in blood pressure and heart rate on the day of PTD. Blood pressure decreased immediately after bilateral PTD and remained low during the monitoring in both cases. A transient decrease in heart rate is also observed just after PTD.

a few hours after PTD (Mahler et al. 1982; Millan et al. 1985), in the present study the hypotensive effect of PTD appeared within a few minutes after the completion of PTD.

Previous experimental results (Brunner et al. 1971; Davis 1977; Maxwell et
S. Sasaki et al. 1977; Freeman et al. 1979) suggest that the renin-angiotensin system may play an important role in the development and maintenance of two-kidney, one clip (2K1C) hypertension in rats, whereas in dogs this system is unlikely to be directly involved in the maintenance of 2K1C hypertension (Watkins et al. 1976; Masaki et al. 1977). The renin-angiotensin system seems to have a major role in the maintenance of 2K1C type hypertension in human (Brown et al. 1966; Brunner and Gavras 1973). However, there are also some pieces of evidence suggesting the involvement of the pressor mechanism other than the renin-angiotensin system in the development and maintenance of RVH. It has been reported that the renin-angiotensin system was not critically involved in the maintenance and even in the development of one-kidney, one-clip (1K1C) hypertension (Brunner et al. 1971; Koletesky et al. 1971; Skeggs et al. 1975; Davis 1977).

It has been reported that the half-life of circulating PRA is within 30 min (Bidani and Churchill 1981; Staessen et al. 1981). Therefore, a rapid decrease in PRA may account for the decrease in BP observed in the initial phase of PTD. However, in the present study, the basal PRA was normal in one case, and in the other case the renin-angiotensin system was inhibited by captopril, an angiotensin I converting enzyme inhibitor. Nevertheless, the hypotensive effect was documented immediately after PTD in both cases. Thus, cardiovascular depressor mechanisms other than inhibition of the renin-angiotensin system seem to be involved in the hypotension induced by PTD at least in the present cases. It has been reported that the sympathetic nervous system does not necessarily contribute to the development of both 2K1C and 1K1C hypertension in animals (Dorr and

![Fig. 3. Averaged systolic (SBP) and diastolic (DBP) blood pressure for 24 hr in several days before, the day and several days after PTD. Significant hypotension after PTD was sustained for the observation period. **p < 0.01 compared to the value of the day before PTD.](image)
Fig. 4. Changes in blood pressure and heart rate just after PTD. In both cases, PTD induced a rapid decrease in blood pressure which was accompanied by a decrease in heart rate.
Recently, several researchers demonstrated that the sympathetic nervous system could contribute to the maintenance of both types of renovascular hypertension (Ayitey-Smith and Varma 1970; Reid et al. 1976; Denoroy et al. 1984; Racz et al. 1986; Salazar et al. 1986).

A rapid decrease in BP may cause reflex tachycardia. However, in the present study the apparent decrease in BP just after PTD was accompanied by a decrease in HR in both cases. It is unlikely that the decrease in HR observed after PTD was mediated by disappearance of the effect of atropine, since the trough of HR after PTD was lower than that before atropine treatment. It is, therefore, concluded that the decrease in HR after PTD may be caused mainly by inhibition of the sympathetic nerve activity at least in the early phase after PTD. However, the possibility remains that the decrease in HR is due to an increase in parasympathetic tone, since in the present study atropine may have not completely inhibited parasympathetic tone.

Recently, Faber and Brody (1985) reported that acute reduction in renal blood flow reflexly induces hypertension through renal afferent nerves when the renin-angiotensin system and the systemic baroreflex function are suppressed. They hypothesized that this reflex mechanism may be particularly important in chronic RVH when the systemic baroreflex or the renin-angiotensin system is impaired. It is noteworthy that established RVH is characterized by a reduced baroreflex sensitivity (Angell-James and George 1980), and by normal or nearly normal PRA (Davis 1977). Thus, it is hypothesized that even in patients with RVH the sympathoexcitatory reflex mechanism through renal afferent nerves may play an important role in the maintenance of RVH and this reflex mechanism may be affected by the change in renal hemodynamics induced by PTD. Katholi et al. (1982) have reported that the hypotension induced by renal denervation or by releasing of renal artery stenosis in rats with 1K1C hypertension was associated with a decrease in peripheral sympathetic nerve activity. Thus, the decrease in HR after PTD observed in the present study may be explained at least in part by the inhibition of the sympathoexcitatory reflex mechanism through renal afferent nerves.

As another possible explanation for the decrease in BP induced by PTD, it is hypothesized that PTD reversed positive sodium and water balance in RVH. However, Otsuka et al. (1979) reported that maintenance of positive sodium balance failed to maintain the 2K1C hypertension after releasing of renal artery stenosis. It has also been reported that the change in urinary sodium and water excretion was independent of cardiohemodynamic changes induced by releasing of renal artery stenosis in rats with both 1K1C and 2K1C hypertension (Liard and Peters 1973). It is also possible that the fall in BP and HR observed in the present study is not a specific response to PTD but simply a nonspecific response to stimulation of the renal artery by PTD manipulation. However, we recently...
observed that when PTD failed to dilate the renal artery stenosis, manipulation of renal artery dilatation did not cause any change in BP and HR (data were not presented).

In short, the present results indicate that the decrease in BP induced by PTD in patients with bilateral renal artery stenosis may be induced either by a decrease in sympathetic tone or by an increase in vagal tone at least just after PTD. These changes in autonomic nervous activity may be mediated centrally through renal afferent nerves in response to rapid changes in renal hemodynamics induced by PTD.

Acknowledgments

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References


