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Vasodilation induced by vasopressin V2 receptor stimulation in afferent arterioles

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Vasodilation induced by vasopressin V2 receptor stimulation in afferent arterioles. We have previously reported that vasopressin (AVP) V2 receptor stimulation increased renal blood flow in dogs anesthetized with pentobarbital. In this study, we examined the direct effects of AVP on afferent arterioles to clarify the role played by V2 receptors in regulating afferent arteriolar tone. We microdissected a superficial afferent arteriole with glomerulus from the kidney of a New Zealand White rabbit. Each afferent arteriole was cannulated with a pipette system and microperfused *in vitro* at 60 mm Hg. The effects of vasoactive substances were evaluated by changes in the lumen diameter of afferent arterioles. We found that AVP decreased the lumen diameter of microperfused afferent arterioles dose-dependently and that a V1 antagonist, OPC21268, inhibited the vasoconstrictor action of AVP. However, AVP 10^{-8} M increased the lumen diameter of norepinephrine (NE)-constricted afferent arterioles pretreated with OPC21268 (OPC+NE, 8.2 ± 0.7 μm; OPC+NE+AVP, 9.9 ± 0.9 μm*; *$P < 0.05$, $N = 13$). This vasodilatory effect of AVP was abolished by pretreatment with a V2 antagonist, OPC31260. Desmopressin (dDAVP), a V2 agonist, increased the lumen diameter of the NE-constricted afferent arterioles (NE, 7.4 ± 0.9 μm; NE+dDAVP, 10.1 ± 0.7 μm*; *$P < 0.05$, $N = 9$). These results suggest that AVP V2 receptors are present in rabbit afferent arterioles and that V2 receptor stimulation induces vasodilation in rabbit afferent arterioles.

The role of AVP in the regulation of renal hemodynamics remains unclear. Low doses of AVP have been reported to increase renal blood flow in dogs anesthetized with pentobarbital [1] and in conscious dogs [2]. Liard [3] reported a slight, but not significant, increase in renal blood flow after 48 hours of water deprivation in conscious dogs. A physiological dose of AVP decreased renal blood flow in anesthetized Brattleboro rats [4]. However, Gellai et al [5] reported that the intravenous infusion of AVP failed to change renal blood flow in conscious Brattleboro rats. The vasoconstrictor effects of AVP show marked regional variations. In particular, the kidney seems to be insensitive to the vasoconstrictor effect of AVP [6, 7]. This renal insensitivity to the vasoconstrictor effect of AVP has been explained by the intrarenal formation of vasodilatory PG(s) [8, 9]. However, recent studies indicate that nitric oxide is actually responsible for the renal dilator action of AVP [10, 11].

In experiments with AVP subtype-selective receptor agonists and antagonists, several lines of evidence indicate that AVP V2 receptors may be involved in local hemodynamic control in some vasculatures. We have already reported that AVP V2 receptor stimulation induced renal vasodilation in dogs anesthetized with pentobarbital [10]. Naitho et al [2] reported that physiological dose of AVP increased renal blood flow and that the V2 antagonist, OPC31260, decreased renal blood flow after 38 hours of water deprivation in conscious dogs. These findings suggest that AVP V2 receptors are present in the resistance vessels of the kidney and that V2 receptor stimulation causes renal vasodilation. However, we must consider other possibilities to explain why V2 receptor stimulation causes renal vasodilation. For example, V2 receptor stimulation may produce some vasodilatory factors within the kidney, or central V2 receptor stimulation may modulate renal sympathetic activity. Therefore, we need to examine the direct effects of V2 receptor stimulation on the renal resistance vessels.

The direct effects of AVP on the resistance vessels in the kidney have recently been examined by several methods. Edwards, Trizna and Kinter [12] reported that, while AVP did not change the lumen diameter of isolated rabbit afferent arterioles, it did decrease the lumen diameter of efferent arterioles via V1 stimulation. However, Weihprecht et al [13] reported that AVP constricted the microperfused rabbit afferent arteriole in a dose-dependent manner. Afferent arteriolar diameter was also decreased by AVP in *in vitro* blood-perfused juxtamedullary nephrons of Sprague-Dawley rats [14]. We do not have a consensus on the effects of AVP on the afferent arteriole. In view of the discrepancy of the effects of AVP on afferent arterioles, we hypothesized that AVP V2 receptors are present on the afferent arterioles and that V2 receptor-mediated renal vasodilation may be responsible for the insensitivity to AVP in the renal circulation. In this study, we examined the direct effects of AVP on isolated microperfused rabbit afferent arterioles and we investigated whether V2 receptor stimulation brings about afferent arteriolar vasodilation.

Methods

Materials

Vasopressin was purchased from the Peptide Institute (Osaka, Japan). Desmopressin was purchased from Sigma Chemical Co. (St. Louis, MO, USA). Bovine albumin fraction V was purchased from Seikagaku Kogyo Co., Ltd. (Tokyo, Japan). OPC21268 and

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OPC31260 were gifts from Otsuka Pharmaceutical (Tokushima, Japan). OPC21268 was dissolved in 20% ethanol and diluted with a modified Krebs-Ringer solution (pH 7.4), containing 105 mM NaCl, 5 mM KCl, 25 mM $NaHCO_3$, 2.3 mM Na_2HPO_4, 10 mM Na acetate, 1 mM $MgSO_4$, 2 mM $CaCl_2$, 8.3 mM glucose, 5 mM alanine, 0.01 mM EDTA, and 10 mM HEPES. The final concentration in the bath medium and perfusate was 0.2% of ethanol. OPC31260 was dissolved in distilled water and diluted with the modified Krebs-Ringer solution.

Isolation and microperfusion of the rabbit afferent arteriole

We used a method similar to that described previously to isolate the afferent arteriole [15, 16]. Male New Zealand White rabbits (1.5 to 2.0 kg) maintained on standard rabbit chow, were anesthetized with intravenous sodium pentobarbital (25 mg/kg), followed by a maintenance dose when necessary, and given an intravenous injection of heparin (500 U, Green Cross, Osaka, Japan). The kidney was exposed through a retroperitoneal flank incision, and the renal pedicle was clamped and cut. The kidney was quickly removed and placed in ice-cold modified Krebs-Ringer solution. Then, the kidney was sliced along the corticomedullary axis. A thin slice was transferred to a dish containing chilled modified Krebs-Ringer solution. The superficial afferent arteriole was dissected free from the surrounding tissues and all tubular fragments were removed under a stereoscopic microscope (SZH; Olympus, Tokyo, Japan) using thin steel needles and sharpened forceps (No.5; Dumont, Switzerland) at 4°C. Great care was taken to avoid touching the vessels and to avoid exerting longitudinal or transverse tension on them. An afferent arteriole with its glomerulus was severed from the interlobular artery by cutting it with a disposable 27-gauge injection needle (TOP; Tokyo, Japan). The arteriole was transferred to a temperature-regulated chamber (ITM; San Antonio, TX, USA) mounted on the stage of an inverted microscope with Hoffman modulation (Diaphot; Nikon, Tokyo, Japan). The volume of the chamber was 1 ml. For drainage, fresh bath medium was supplied to the bottom right side of the chamber at 0.5 ml/min and medium was gently aspirated from the top of the left side of the chamber. The bath medium was identical to the dissection solution, and was bubbled with 95% O_2 and 5% CO_2. During the experiment, water-saturated gas (90% O_2 and 10% CO_2) was gently blown over the surface of the bath to maintain the pH at 7.4.

A schematic illustration of the micropipette system is shown in Figure 1 and a photograph of a microperfused afferent arteriole with its glomerulus is shown in Figure 2. The method used for cannulating the afferent arteriole into the micropipette system is similar to that reported by Osgood et al [17] and by Ito and Carretero [18]. One end of the afferent arteriole was drawn into the holding pipette, which had a constriction (internal diameter, about 20 μm). The tip of the perfusion pipette (outer diameter, about 12 μm) was advanced into the lumen of the afferent arteriole. A stronger vacuum was then applied to the holding pipette to pull the afferent arteriole further toward the constriction in the holding pipette and thereby seal it between the two pipettes. Microperfusion of the afferent arteriole was carried out by the method described by Ito et al [18, 19], perfusate with oxygenated modified Krebs-Ringer, containing 5% bovine serum albumin, being used. The pressure pipette (outer diameter, approximately 3 μm), which was filled with NaCl solution containing 5% FD&C green and 4% KCl, was then advanced into the afferent arteriole

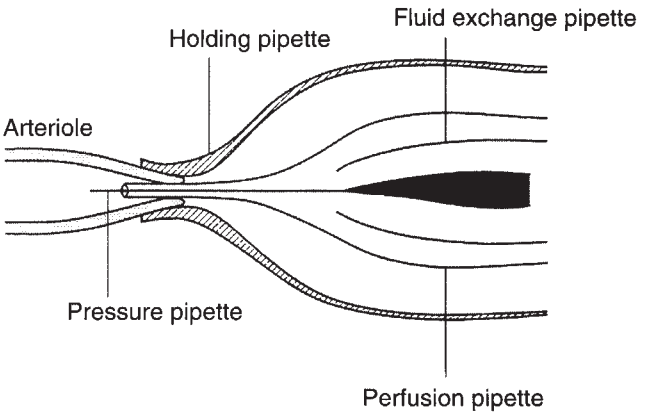

Fig. 1. *Schematic illustration of pipette system.*

through the opening of the perfusion pipette. The intraluminal pressure was measured by Landis' technique [17] using this pressure pipette. The pressure at which neither the colored solution flowed into the afferent arteriole nor the intraluminal fluid flowed into the pressure pipette was regarded as being equal to the pressure in the afferent arteriole. After the completion of cannulation, the intraluminal pressure was set at 60 mm Hg and maintained throughout the experiment. The intraluminal pressure was continuously monitored with a pressure transducer and monitor (Digic VPC, Valcom, Tokyo, Japan). Major leaks of fluid could be seen because of the different refractile properties of the perfusate and bath solution. If the intraluminal pressure was not maintained at constant level, the experiment was discarded. Microdissection and cannulation of the afferent arteriole were completed within 90 minutes. The temperature of the bath was gradually raised to 37°C and monitored during the experiment (E5CS; Omron, Tokyo, Japan). A 30-minute equilibration period was allowed before each experiment. The image of the afferent arteriole during the experiment was recorded with a video system that consisted of a camera adapter and CCD camera and control unit (CCD-10; Olympus, Tokyo, Japan), a monitor (NV-0930Z; Mitsubishi, Tokyo, Japan), and a video recorder (TIMELAPSE BR-9000; JVC, Tokyo, Japan). The lumen diameter of the afferent arteriole was measured directly on the video monitor screen. The lumen diameter of afferent arteriole was measured at the most constricted point and repeated measurements were made at this same point. Following the 30 minute equilibration, measurements of the lumen diameter were made at one minute intervals for three minutes. During the measurements, we confirmed that the lumen diameter of afferent arteriole was stable. If the lumen diameter was not stable, the results of the experiment were discarded. At the end of the experiment, the viability of the vessel was assessed by the response to 10^{-5} M norepinephrine (NE).

Experimental protocols

Effect of AVP on the lumen diameter of afferent arterioles. Following 30 minutes of equilibration, AVP was applied to the bath in increasing concentrations, to determine the dose-response curve of AVP. The continuous bath exchange was stopped and the bath medium was rapidly exchanged for the medium containing the lowest concentration of AVP (10^{-12} M). The bath exchange

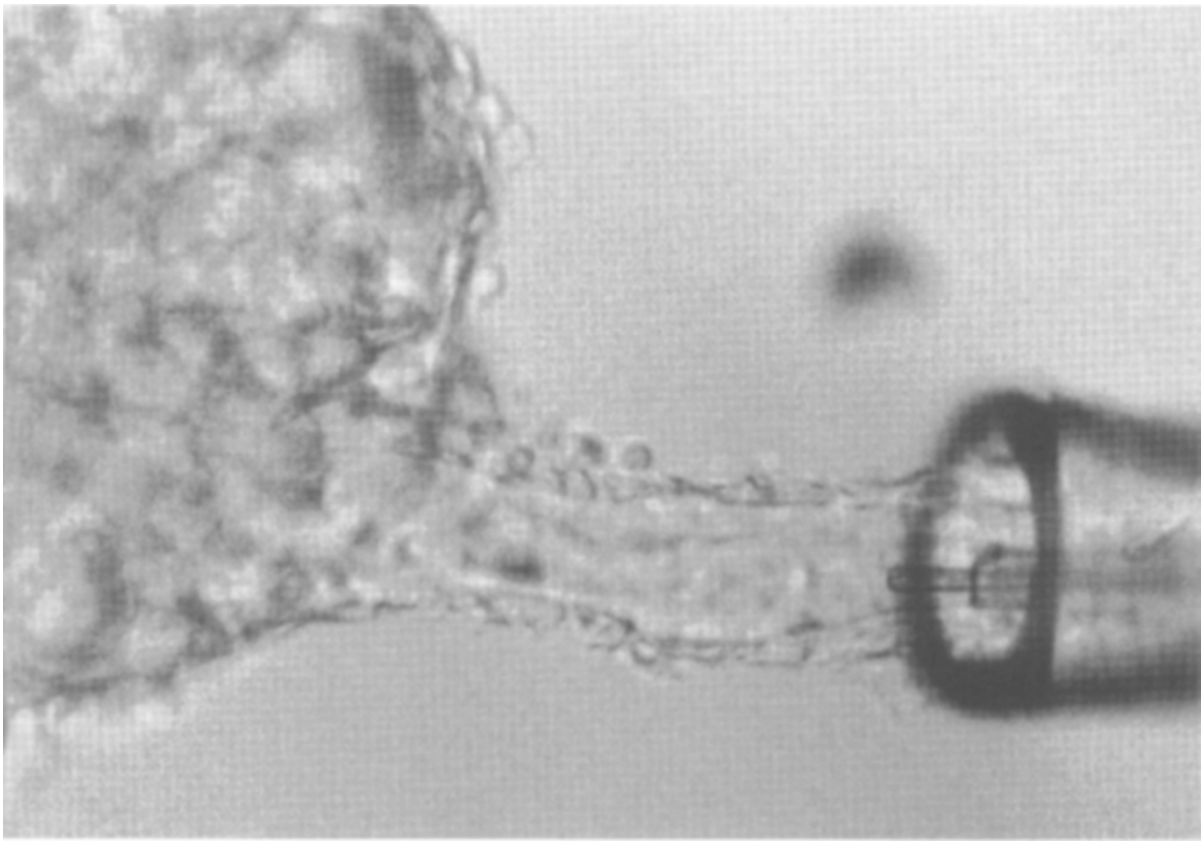

Fig. 2. *A microperfused afferent arteriole with glomerulus.*

was resumed with medium containing the same concentration of AVP and the arteriole was observed for three minutes. Every three minutes, the concentration of AVP was increased by one order of magnitude, up to 10^{-6} M. The control value of the lumen diameter was measured immediately before we added the lowest concentration of AVP. The lumen diameter of the afferent arteriole was measured one to two minutes after the addition of AVP.

In another experiment, we applied a single dose of AVP 10^{-8} M after the control measurement. We wanted to examine the possibility of tachyphylaxis in response to AVP, since even the highest dose of AVP 10^{-6} M caused weak contraction in 4 of 12 afferent arterioles during the cumulative addition. After we had observed the effect of a single dose of AVP application on the lumen diameter for three minutes, the arteriole was washed with plain modified Krebs-Ringer at least 10 times and the bath was continuously exchanged with fresh bath medium for approximately 30 minutes. After a 30-minute equilibration period, we added OPC21268 (a non-peptide V1 antagonist, 10^{-5} M) [20] to the perfusate and bath medium. Following 30 minutes of pretreatment with OPC21268, AVP 10^{-8} M was added to the bath. The effects of AVP on the lumen diameter were evaluated in the manner indicated above.

Effect of AVP 10^{-8} M on the lumen diameter of norepinephrine (NE)-constricted afferent arterioles pretreated with AVP antagonists. We examined whether V2 receptor stimulation increased the lumen diameter of microperfused rabbit afferent arterioles. After the microperfusion of isolated afferent arterioles was completed, we added a V1 antagonist (OPC21268 10^{-5} M) to the perfusate and bath medium. Following 30 minutes of pretreatment with OPC21268, we added NE to the bath medium and afferent arterioles were preconstricted to approximately 50% of the basal

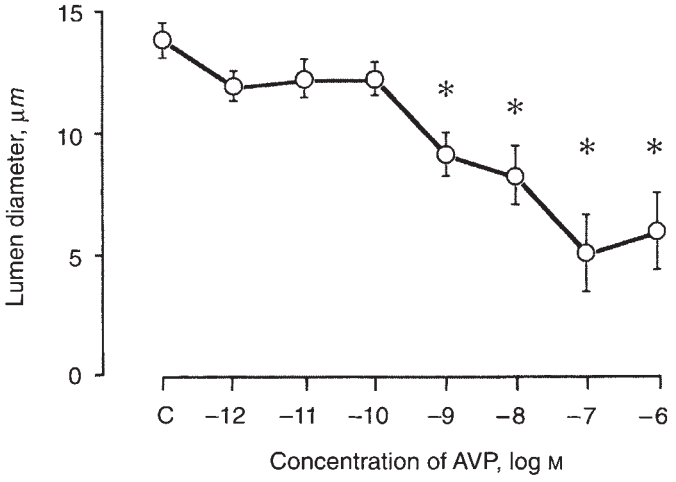

Fig. 3. *Dose-response effects of vasopressin (AVP) on the lumen diameter of afferent arterioles (N = 12).* Abbreviation C is control. *$P < 0.05$, compared with the control.

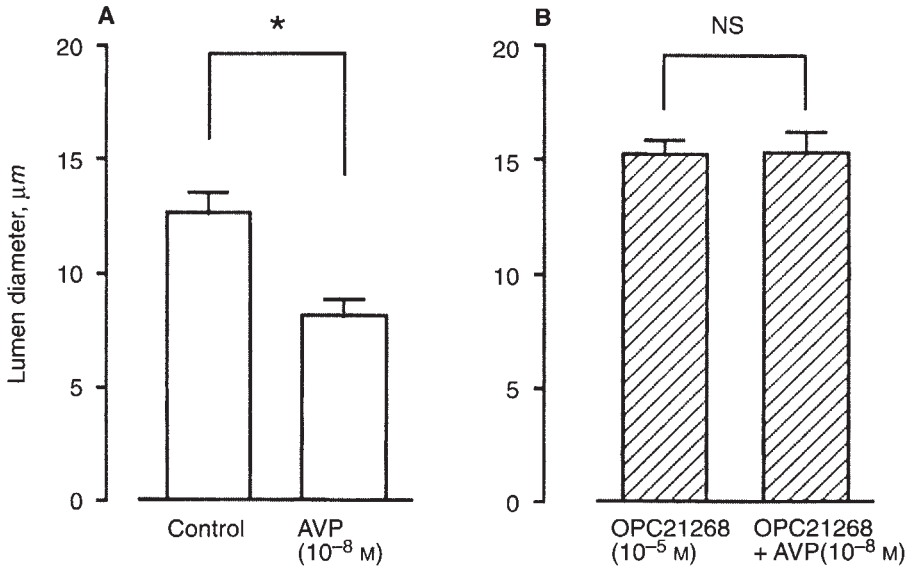

Fig. 4. A. *Effects of vasopressin (AVP; 10^{-8} M) on the lumen diameter of afferent arterioles (N = 8).* $^{*}P < 0.05$. **B.** Effects of vasopressin (AVP; 10^{-8} M) on the lumen diameter of afferent arterioles pretreated with a non-peptide V1 antagonist, OPC21268 10^{-5} M (N = 5).

diameter (mean concentration of NE; 3.5×10^{-7} M). After we had confirmed that lumen diameter was stable, AVP 10^{-8} M was added to the bath medium and changes observed in the lumen diameter for five minutes. The lumen diameter of the afferent arteriole was measured one to two minutes after the application of AVP.

In another experiment, following 30 minutes of pretreatment with OPC21368 (10^{-5} M) and OPC31260 (a non-peptide V2 antagonist and weak V1 antagonist, 10^{-5} M) [21], we preconstricted the arteriole with NE in the manner described above. The effects of AVP 10^{-8} M on the lumen diameter of the afferent arterioles were then evaluated.

Effects of desmopressin (dDAVP, 10^{-8} M) on the lumen diameter of afferent arterioles. After a 30-minute equilibration period, we examined the effects of dDAVP 10^{-8} M on the lumen diameter of afferent arterioles. dDAVP 10^{-8} M was added to the bath medium and the changes in lumen diameter were observed for five minutes. The control value of the lumen diameter was measured immediately before dDAVP was added. The lumen diameter of the afferent arteriole was measured one to two minutes after the addition of dDAVP. The afferent arteriole was washed with plain modified Krebs-Ringer at least 10 times and the bath was continuously exchanged with fresh bath medium for about 30 minutes. Then the effects of dDAVP 10^{-8} M on the lumen diameter of NE-constricted afferent arterioles were examined.

After a 30-minute equilibration period, the vessel tone of the afferent arteriole was increased by NE. dDAVP 10^{-8} M was added to the bath medium after we had confirmed that the lumen diameter was stable. Changes in the lumen diameter were observed for five minutes. The effects of dDAVP on the lumen diameter were evaluated in the manner described above.

Data analysis

Values are expressed as means ± SEM. Statistical analyses were performed with Student's paired t-tests for two groups. The data were analyzed by one-way analysis of variance, followed by a least significant difference test for more than three groups. $P < 0.05$ was considered a statistically significant difference.

Results

Effect of AVP on the lumen diameter of afferent arterioles

The basal lumen diameter of microperfused afferent arterioles was 14.1 ± 0.4 μm (N = 20). AVP decreased the lumen diameter of afferent arterioles dose-dependently (Fig. 3). We observed strong constriction of lumen diameter at the highest dose of AVP (10^{-6} M). However, in 4 out of 12 experiments, the lumen diameter only decreased by a small percentage of the control diameter at this particular concentration during the cumulative application of AVP. A single dose of AVP (10^{-8} M) decreased the lumen diameter from 12.5 ± 0.9 to 8.0 ± 0.7 μm (N = 8; Fig. 4A). A single addition of AVP 10^{-8} M decreased the lumen diameter by 36%, and the cumulative addition of AVP 10^{-8} M decreased the lumen diameter by 40%, that is, AVP 10^{-8} M decreased the lumen diameter of afferent arterioles similarly in both types of additions. After pretreatment with the V1 antagonist, OPC21268 10^{-5} M, AVP 10^{-8} M did not change the lumen diameter (before AVP, 15.2 ± 0.7 μm; after AVP, 15.3 ± 0.9 μm; N = 5; Fig. 4B).

Effect of AVP 10^{-8} M on the lumen diameter of NE-constricted afferent arterioles pretreated with AVP antagonists

After pretreatment with OPC21268 10^{-5} M, AVP 10^{-8} M increased the lumen diameter of NE-constricted afferent arterioles (Figs. 5 and 6A). However, AVP 10^{-8} M did not change the lumen diameter of NE-constricted afferent arterioles that were pretreated with OPC21268 10^{-5} M and OPC31260 10^{-5} M (Fig. 6B). These results suggest that AVP increased the lumen diameter of NE-constricted afferent arterioles via V2 receptor stimulation.

Effects of desmopressin (dDAVP, 10^{-8} M) on the lumen diameter of afferent arterioles

dDAVP 10^{-8} M, a V2 agonist, did not change the lumen diameter of microperfused rabbit afferent arterioles (Fig. 7A). We also confirmed that higher concentrations of dDAVP (up to 10^{-6} M) did not decrease the lumen diameter of afferent arterioles (data not shown). dDAVP 10^{-8} M increased the lumen diameter

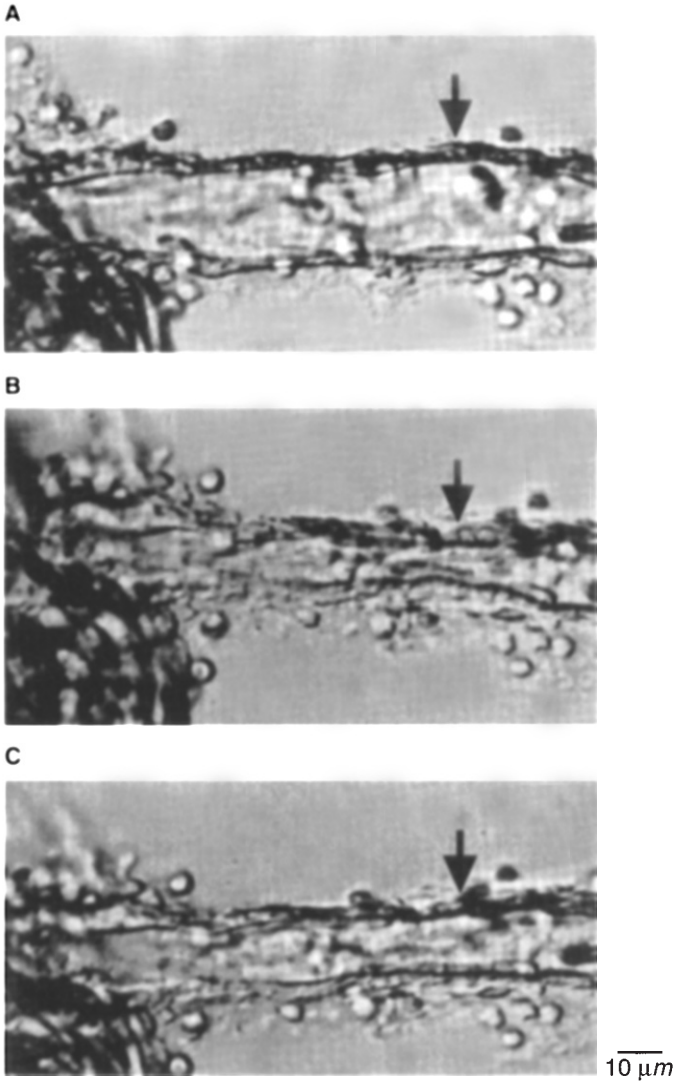

Fig. 5. *An example of changes in the diameter of an afferent arteriole (AA) pretreated with the non-peptide V1 antagonist, OPC21268 10^{-5} M.* Control condition of OPC21268 treated-AA (**A**); norepinephrine (NE) decreased the lumen diameter of the AA (**B**); vasopressin 10^{-8} M increased the lumen diameter of the NE-constricted AA pretreated with a V1 antagonist (**C**). Arrows indicate where measurements were made.

of microperfused rabbit afferent arterioles preconstricted with NE (mean concentration, 4×10^{-7} M) from 7.4 ± 0.9 to 10.1 ± 0.7 μm ($N = 9$; Figs. 7B and 8).

Discussion

We have already reported that an intrarenal infusion of AVP increased renal blood flow in dogs pretreated with OPC21268, a non-peptide V1 antagonist [10]. However, in that study we could not clarify whether this V2-mediated renal vasodilation was caused by the direct stimulation of V2 receptors on the renal resistance vessels. In this present study, we investigated whether AVP V2 receptor stimulation caused the vasodilation of isolated rabbit microperfused afferent arterioles. We demonstrated that AVP increased the lumen diameter of NE-preconstricted microperfused rabbit afferent arterioles pretreated with a non-peptide V1 antagonist, OPC21268, and that a non-peptide V2 antagonist, OPC31260, abolished this vasodilatory action of AVP. We also demonstrated that desmopressin, a V2 agonist, increased the lumen diameter of NE-preconstricted afferent arterioles. These results suggest the presence of vasopressin V2 or V2-like receptors on rabbit afferent arterioles, and also suggest that V2 or V2-like receptor stimulation causes vasodilation in the rabbit afferent arterioles.

AVP is known to produce powerful vasoconstriction in *in vitro* experiments. However, in *in vivo* experiments, intravenously injected AVP does not show a strong pressor action. This weak pressor action is explained by its buffering effects; AVP decreases cardiac output and enhances baroreflex sensitivity. Recent developments of AVP receptor subtype agonists and antagonists has enabled us to evaluate the role played by V2 receptors in regulating systemic and regional hemodynamics. It has been shown that AVP decreased total peripheral resistance in the presence of a V1 antagonist in conscious dogs while a V2 agonist, 4-valine-8-D-AVP, decreased total peripheral resistance in these animals [22]. Desmopressin, a V2 agonist, increased cardiac output and decreased total peripheral resistance in conscious dogs. These changes were prevented by pretreatment with a combined V1-V2 antagonist [23]. It has been reported that the intraarterial infusion of AVP into the brachial artery increased human forearm blood flow and desmopressin also increased human forearm blood flow [24, 25]. Desmopressin is used for the treatment of diabetes insipidus and one of its major side effects is reported to be hypotension [26]. These findings suggest that the V2 agonistic properties of AVP may restrict the hypertensive action of this hormone. In the kidney, physiological doses of AVP increased renal blood flow in animal experiments [1, 27]. We have reported that the intrarenal infusion of AVP increased renal blood flow in dogs pretreated with a V1 antagonist [10]. Naitoh et al [2] reported that deprivation of water for 36 hours increased the plasma concentration of AVP and increased renal blood flow in conscious dogs. They also observed that OPC31260, a non-peptide V2 antagonist, decreased renal blood flow after the 36 hours of water deprivation. However, they did not deny the possibility that the indirect effects of AVP caused V2 receptor-mediated renal vasodilation. For example, it has been reported that AVP reduced the renal sympathetic nerve activity through the central nervous system [28]. Unger et al [29] reported that AVP sensitized the baroreceptor reflex through V2 receptors. Reduced renal sympathetic nerve activity through the central nervous system may cause renal vasodilation. In this study, we demonstrated that V2 or V2-like receptor stimulation increased the lumen diameter of microperfused rabbit afferent arterioles. Our results thus indicate that V2 receptor mediated renal vasodilation at least in part is caused by the direct stimulation of vascular V2 receptors.

There is no consensus regarding the effects of AVP on the afferent arteriole. Edwards, Trizna and Kinter [12] reported that, although AVP did not change the lumen diameter of isolated rabbit afferent arterioles, it did decrease the lumen diameter of efferent arterioles via V1 stimulation. However, Weihprecht et al [13] reported that AVP constricted the microperfused rabbit afferent arteriole in a dose-dependent manner. Neither of these investigators considered the possible participation of V2-receptor mediated vasodilation in regulating arteriolar tone during the application of AVP. Our findings on the effect of AVP on the lumen diameter of afferent arterioles are consistent with those of

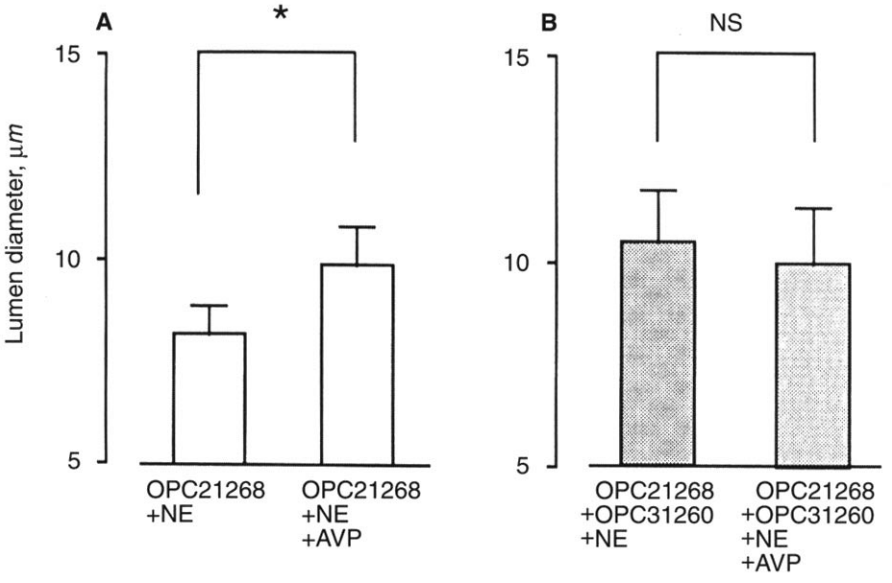

Fig. 6. A. *Effect of vasopressin (AVP; 10^{-8} M) on the lumen diameter of norepinephrine (NE)-constricted afferent arterioles pretreated with the non-peptide V1 antagonist, OPC21268 (10^{-5} M) ($N = 13$). *$P < 0.05$.* **B.** Effect of AVP 10^{-8} M on the lumen diameter of NE-preconstricted afferent arterioles pretreated with the V1 antagonist, OPC21268 10^{-5} M, and the V2 antagonist,OPC31260 10^{-5} M ($N = 6$).

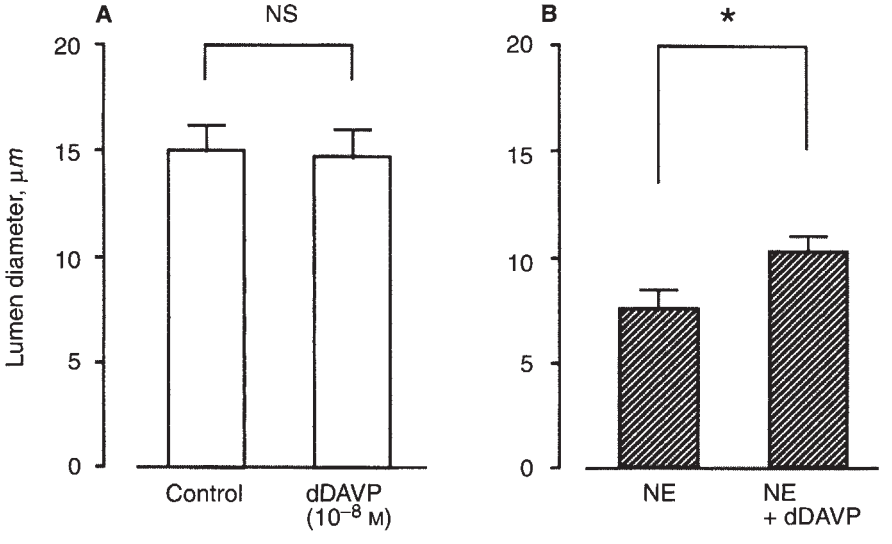

Fig. 7. A. *Effects of desmopressin (dDAVP, 10^{-8} M) on the lumen diameter of afferent arterioles ($N = 5$).* **B.** Effects of dDAVP 10^{-8} M on the lumen diameter of norepinephrine (NE)-preconstricted AA ($N = 9$). *$P < 0.05$.

Weihprecht et al [13]. However, we observed that even the highest dose of AVP (10^{-6} M) decreased the lumen diameter by only a small percentage of the control value in 4 of 12 afferent arterioles during the cumulative addition of AVP. These weak vasoconstrictor effects of AVP may be explained in terms of V2 receptor-mediated renal vasodilation. This V2 receptor-mediated arteriolar vasodilation may explain the discrepancy between the finding of Edwards et al [12] and those of Weihprecht et al [13].

In this study, we found that AVP decreased the lumen diameter of isolated microperfused rabbit afferent arterioles in a dose-dependent manner. Therefore, we cannot fully explain the renal insensitivity to the vasoconstrictor effects of AVP in terms of V2-mediated afferent arteriolar vasodilation. It has been reported that AVP increased urinary and effluent prostaglandin E2 in the isolated perfused kidney [30, 31]. Oliver et al [1] indicated that physiological concentrations of AVP increased renal blood flow and that the renal vasodilation was mediated by renal prostaglandins. V1 receptor stimulation is reported to produce vasodilatory PG(s) in several types of cells in the kidney, for example, in interstitial cells [8], mesangial cells [32] and renal tubular cells [9]. A recent study indicated that inhibition of nitric oxide synthesis eliminated renal vasodilation induced by subpressor doses of AVP [11]. The AVP-stimulated production of vasodilatory PG(s) and/or nitric oxide within the kidney may play an important role in the renal insensitivity to the vasoconstrictor effects of AVP.

Several lines of evidence have recently suggested that the vasodilatory mechanism of AVP V2 receptor stimulation involved the nitric oxide production pathway. We have already reported that N^G-nitro-L-arginine, a nitric oxide synthase inhibitor, attenuated V2-receptor-mediated renal vasodilation [10], and it has been shown that N^G-monomethyl-L-arginine, a blocker of nitric oxide synthase, inhibited AVP-induced vasodilation in the human

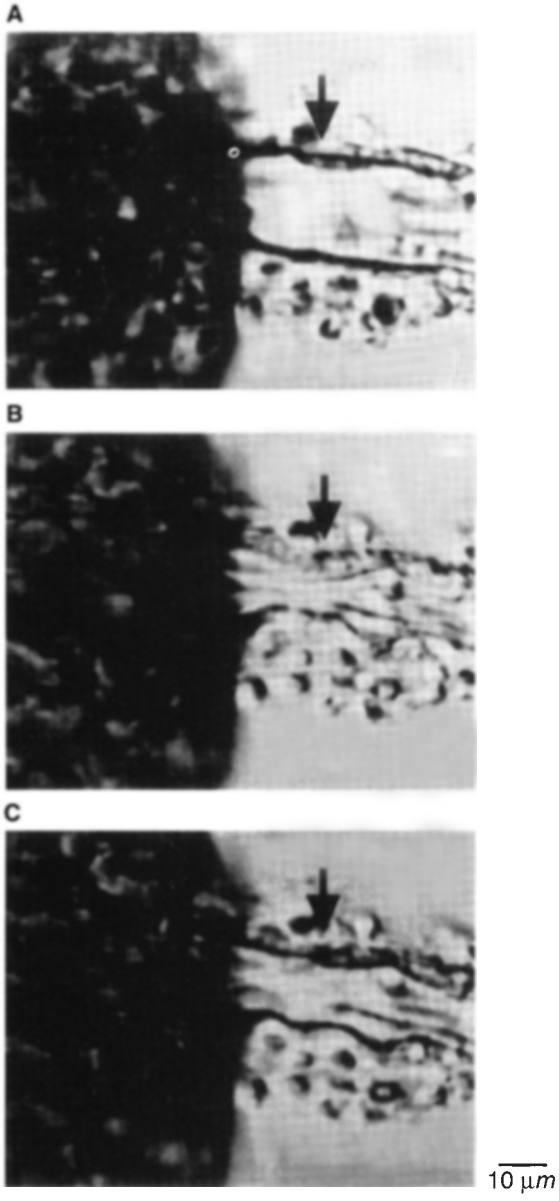

Fig. 8. *An example of arteriolar response to desmopressin (10^{-8} M).* Control condition of afferent arteriole (AA)(**A**); norepinephrine (NE) decreased the lumen diameter of the AA (**B**); desmopressin (10^{-8} M) increased the lumen diameter of the NE-constricted AA (**C**). Arrows indicate where measurements were made.

forearms [33]. It has also been reported that the hemodynamic effects of selective V2 agonists were blunted by the systemic administration of N^G-nitro-L-arginine methyl ester, a blocker of nitric oxide synthase, in dogs [34]. Thus, it appears that V2 receptor stimulation may act to liberate nitric oxide in isolated afferent arterioles, resulting in arteriolar vasodilation. The mechanisms responsible for the V2 receptor-mediated afferent arteriolar vasodilatory effects remain to be clarified.

In summary, AVP decreased the lumen diameter of microperfused rabbit afferent arterioles, and a V1 antagonist, OPC21268, inhibited the vasoconstrictor action of AVP. However, AVP increased the lumen diameter of norepinephrine-constricted afferent arterioles pretreated with OPC21268. This vasodilatory effect of AVP was abolished by pretreatment with a V2 antagonist, OPC31260. Desmopressin, a V2 agonist, increased the lumen diameter of NE-constricted afferent arterioles. Our findings suggest that AVP V2 or V2-like receptors are present on rabbit afferent arterioles and that V2 or V2-like receptor stimulation induces vasodilation in these arterioles.

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