Japanese Journal of Physiology, **46**, 83–92, 1996

Sympathoadrenal Activity in the Visceral (Viscerovascular) Reflexes to Distension of the Urinary Bladder

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Abstract: Distension of the urinary bladder can cause reflex pressor responses, which appear to be mediated by increased sympathetic activity. We correlated the involvement of the adrenal gland (medulla) itself and adrenosympathetic nerve activities with the viscerovascular reflexes and their role in controlling the reflex response following distension of the urinary bladder. The experiments were performed in 37 chloralose anesthetized cats. It was observed that reflex rise of blood pressure was not affected by intravenous administration of propranolol, indicating that the β-adrenoceptors (inhibitory effect) were not involved in such reflex. Phentolamine, hexamethonium and guanethidine sulfate completely prevented the reflex action, and comparison of the magnitudes of responses and this inhibitory effect suggests the participation of α-adrenoceptors (excitatory effect) as a result of the vasoconstriction that develops during bladder distension. In the present study, we determined that adrenalectomy significantly ($p<0.0001$) altered the magnitudes of reflex response during bladder distension. The 10.4% (systolic, $p<0.001$) and 10.6% (diastolic, $p<0.01$) change in reflex response was mediated directly through adrenomedullary catecholamines, and the 14.8% (systolic, $p<0.001$) and 23.8% (diastolic, $p<0.0001$) change in vasopressor response was mediated by adrenosympathetic ganglionic activity. The single unit activity from the central cut end of the adrenal sympathetic nerve was recorded for direct evidence. An increase in electrical activity (1–3 to 7–10 spikes/s; $p<0.001$) of the adrenal sympathetic nerve with the rise of blood pressure during bladder distension was observed. We concluded that, like other sympathetic nerves, the adrenal sympathetic nerve contributed to the enhancement of blood pressure during bladder distension. This result also explains the partial inhibition of reflex hypertension during bladder distension after adrenalectomy. These studies also conclude that the adrenal gland and adrenosympathetic nerve act as facilitatory modulators in maintaining catecholamine secretion under conditions of stress (urinary bladder distension). [Japanese Journal of Physiology, 46, 83–92, 1996]

Key words: adrenal gland, adrenosympathetic nerve, vasoconstriction, urinary bladder, visceral reflex.

Gastrointestinal obstruction or retention of urine may induce stress and become the causative factor for cardiovascular abnormalities. The hypertensive effect due to distension of the urinary bladder has been known for a long time [1]. Further investigations have, however, been made on the positive pathways and mechanisms of these reflexes [2–7]. Guttmann and Whitteridge [8] have observed a marked rise of blood pressure, which is characterized by greater systolic elevation, in paraplegic patients with spinal lesions above T_5 than in patients with lesions at lower levels. Splanchnic vasoconstriction has been reported to be the cause of such a viscerovasopressor response [4, 9–13], and it achieved the response by activation (excitation) of the vesicosympathetic nerve. Recently, we found that the spleen, as well as the splenic and

Received on May 8, 1995; accepted on January 16, 1996
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splanchnic sympathetic nerves, is directly involved in modulation of viscerovascular reflexes induced by urinary bladder distension [7]. The complete suppression of the reflex rise of blood pressure during bladder distension after sectioning of the splanchnic nerve and the increased bioelectric activity of the single unit preparation of the splanchnic nerve [7] justified recording of the bioelectric activity of the adrenal sympathetic nerve with single fiber unit preparation, since the latter is presumed to be a branch of the splanchnic nerves. The direct experimental evidence of the involvement of adrenal glands and the adrenosympathetic nerve in the visceral (viscerovascular) reflex is still unknown. Therefore, the aim of this study was to determine: (*i*) the involvement and active participation of the adrenal gland (medulla) itself, and (*ii*) the reflex reaction of single unit fiber from the adrenosympathetic efferent nerve activity in the visceral reflexes following distension of the urinary bladder.

MATERIALS AND METHODS

General procedures. Experiments were performed in 37 healthy, adult cats of either sex, each weighing 3–4 kg. Food, but not water, was withheld for 20 h before experimentation. The animals were anesthetized with α-chloralose (60–70 mg/kg, IV) after initial induction with anesthetic ether. The trachea was exposed and a T-shaped polyethylene cannula was inserted into the trachea after a low tracheotomy for free breathing and also for artificial ventilation with a Starling-Ideal-Respiratory pump (INCO Ambala, India), if required. A thermistor was connected with the tracheal T-tube for monitoring respiration through a Beckman RM Dynograph (Beckman Instruments). Variations in the temperature of the inspired and expired air, recorded on a Beckman RM Dynograph via the thermistor, indicated the respiratory rate. A femoral vein access line was established for constant infusion of saline and anaesthetic. Normal physiological saline (0.9% w/v NaCl solution) with 5% glucose was administered by drip infusion into the femoral vein to maintain body fluid and stabilize the preparation. Core body temperature was maintained at 37–38°C by a hot-water-circulating heating pad underneath the cat, and by a feedback controlled heat lamp (thermoprobe inserted into the thoracic esophagus). Body temperature and blood pH were checked from time to time and maintained within the normal range. At the end of the experiments, the cats were killed with an overdose of intravenous pentobarbital.

Recording of blood pressure. The right femoral artery was cannulated with a polyethylene catheter and was connected with a three-way stopcock (Pharmaseal, USA) to a Bell & Howell (Type 4-327-0129) pressure transducer filled with heparin-saline solution (100–150 IU/ml). Blood pressure was recorded on a Beckman RM Dynograph after initial amplification through the Beckman V/P/Pressure coupler (Type 9853A). Blood pressure and body temperature were monitored within the normal range.

Recording of intravesical pressure. The urethra was exposed through a midline suprapubic incision of the lower abdomen and cleared of surrounding tissues. The bladder was cannulated with a polyethylene catheter via the urethra in order to change bladder volume and monitor intravesical pressure [7, 14]. The catheter was connected to a T-tube, one end of which was connected with a pressure transducer while the other end was used for distension (40–50 ml) of the bladder with normal, warm (37°C) saline [7]. The bladder was distended rapidly and kept distended for 90 s; the bladder was evacuated just after 90 s. The intravesical pressure rose sharply during distension and attained a height of 50–60 mmHg but was immediately followed by a fall to 30–40 mmHg at the completion of filling and it remained at that level as long as the bladder was kept distended [7].

Adrenalectomy. Adrenalectomy was performed as described by Armitage [15]. A longitudinal incision was made on the midline of the abdominal wall of the anesthetized cats. The adrenal veins and arteries were isolated carefully with the aid of a stereoscopic dissecting microscope (Vickers, UK). When the adrenal glands were excluded from the circulation, double ties were placed around the adrenal veins and the adrenal arteries, and the glands were usually removed completely under the microscope. In a few experiments, the right adrenal gland was so close to the vena cava that the veins and arteries were tied but the gland was left *in situ*. The animals were allowed to rest at least 60 min after the surgical procedure.

Isolation of adrenosympathetic nerves, single fiber preparation and recording. The complete preparations were performed under a stereoscopic dissecting microscope. The left adrenal gland and its innervation were exposed carefully. Suitable lengths of the adrenosympathetic nerves were cleared and isolated from the surrounding tissues carefully and a fine loop was made around each nerve. The nerve was raised by pulling the loop and sectioned when necessary. The nerve was stabilized by placing it on a black ebonite dissecting plate in a warm paraffin pool. A small length of adrenosympathetic nerve was desheathed and split into fine filaments and was

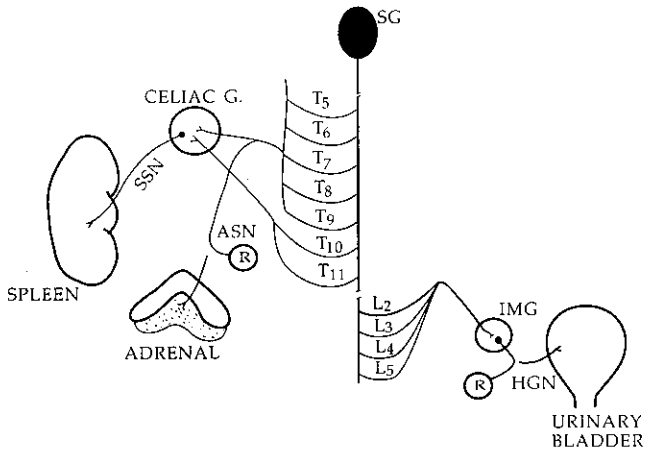

Fig. 1. Schematic diagram showing the recording site (R) of the left adrenosympathetic nerve (ASN) and hypogastric nerve (HGN). SG=stellate ganglion; CELIAC G.=celiac ganlion; SSN=splenic sympathetic nerve; HGN=hypogastric nerve; IMG=inferior mesenteric ganglion; T_1–T_{11}=thoracic sympathetic rami.

emerged in liquid paraffin. A bipolar silver-silver chloride electrode was used to record single fiber unit activity. The split nerve filaments from the central cut end were laid across one silver-silver chloride electrode, and the other electrode was used for balancing with some other tissue strand [16]. Single unit activity was displayed on a dual beam oscilloscope (5112, Tektronix Inc., USA), after initial amplification through a differential amplifier for monitoring sound. The single unit activity was confirmed by checking the height and contour of the spike in a fast beam sweep. The unit responses to urinary bladder distension were then studied and the activity was stored on a thermionic tape recorder (4FM tape recorder, Recal-Thermionic Ltd., Southampton, UK). The profile of the recording system is shown diagrammatically in Fig. 1.

Spinal cord transection. The transection of the spinal cord at the level of S_1–S_4 vertebrae was performed following the methods of Koley and Mukherjee [17]. The spinal cord was opened by laminectomy and before transection 2% lidocaine was injected in the cord at S_1–S_4 level to avoid shock. The animals were maintained with artificial respiration, if and when required, and 5% glucose saline was administered by drip infusion into the femoral vein to maintain body fluid.

Denervations of hypogastric and pelvic nerves. The hypogastric and pelvic nerves were exposed retroperitoneally as described by Floyd *et al.* [18, 19]. The separation of nerves and bilateral denervation were performed under a steroscopic dissecting microscope (Vicker's, UK) after placing an ice cube over the nerves to prevent cardiac shock.

Local anaesthesia of ganglion. Before denervation of hypogastric nerve, the inferior mesenteric ganglion was anaesthetised by local anaesthesia with gesicain (lidocaine hydrochloride, 2%) in order to check the involvement of hypogastric nerves in the rise of blood pressure during bladder distension. In this condition, the blood pressure during bladder distension was recorded.

Single fiber preparation and recording of hypogastric sympathetic nerves. The hypogastric nerves were exposed retroperitoneally as described by Floyd *et al.* [18]. The nerves were also cleaned from the surrounding connective tissues and sectioned below the inferior mesenteric ganglion and then immersed in paraffin. The single fiber preparation and recording techniques were adopted as adrenosympathetic nerve recording.

Statistics. Results are expressed as mean±standard error of mean (SEM). The significance of differences between groups was estimated with Student's *t*-test. Each mean value was the average of 10 animals.

Drugs used. Propranolol hydrochloride (ICI), phentolamine mesylate (Rogitine, Ciba-Geigy), guanethidine sulfate (Ciba-Geigy), and hexamethonium bromide (Koch-Light Lab), in physiological saline solution, were used.

RESULTS

Effect of propranolol, phentolamine, guanethidine sulfate and hexamethonium on blood pressure induced by urinary bladder distension in non-adrenalectomized (adrenal intact) animals

In chloralose anesthetized cats, the normal systolic (SBP) and diastolic (DBP) blood pressure was 140±5 mmHg and 115±3 mmHg, respectively. The rapid distension of the urinary bladder with warm (37°C) normal saline (60 ml) caused an increase in SBP and DBP to a maximum of 173±3 mmHg (23.6%, $p<0.0001$) and 151±3 mmHg (31.3%, $p<0.0001$), respectively, with the rise of mean blood pressure being 32–35 mmHg (Fig. 2). The elevation of SBP and DBP continued during the 90-s period of bladder distension, but the increased blood pressure reached the maximum level at 60 s of distension. It was found that administration of propranolol (1 mg/kg IV) does not affect the excitatory bladder response or the blood pressure following bladder distension. This observation indicates that this response is not mediated via β-adrenoceptor activation. The administration of phentolamine (2.5 mg/kg), guanethidine sulfate

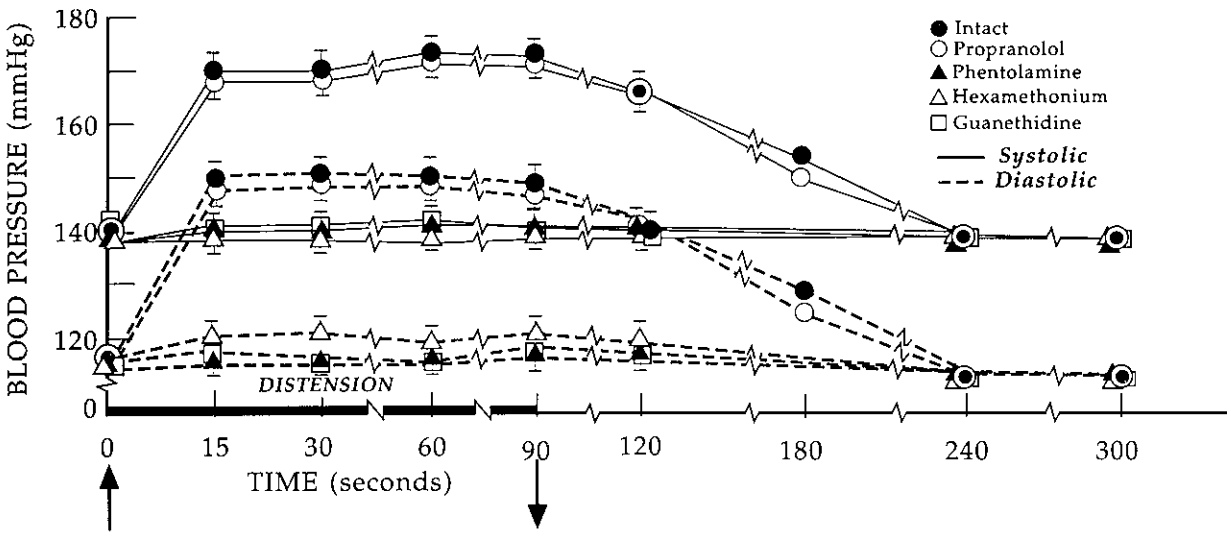

Fig. 2. Response pattern of average systolic and diastolic blood pressure to bladder distension in cat, intact (control) and pretreated with propranolol (1 mg/kg), phentolamine (2.5 mg/kg), hexamethonium (1 mg/kg), and guanethidine sulfate (20 mg/kg). Results are mean±SEM (n=10). The distension period is indicated by the arrows (↑↓). In intact and propranolol, the complete recovery time is 2 min 30 s. The effects of the other drugs (phentolamine, hexamethonium and guanethidine) did not recover with time.

(20 mg/kg) and hexamethonium (1 mg/kg) strongly counteract (p<0.001) the vasopressor response during bladder distension (Fig. 2) and the SBP/DBP were 146±2/115±2, 142±2/116±2 and 142±2/118±2 mmHg, respectively, for each drug. After evacuation of the bladder at 90 s, the increased pressor response due to distension (in intact and propranolol) at resting level at 240 s. The total time from evacuation until resting blood pressure returned to normal is 150 s, but the effect of the other drugs (phentolamine, hexamethonium and guanethidine) remained the same (Fig. 2).

Changes in blood pressure following urinary bladder distension in adrenalectomized animals

In those animals where the adrenal glands were ligated/removed surgically, the resting blood pressure was 135±2/135±3 mmHg (SBP) and 110±3/109±3 mmHg (DBP), respectively. The change in resting pressure (SBP: 3.6% and DBP: 5.2%) due to adrenal vein ligation or adrenal gland removal was not significant (SBP: p=0.4024, DBP: p=0.1744). In adrenalectomized animals, maximum pressure response, i.e., systolic and diastolic pressure was found to be 155±3 (14.8%, p<0.001) and 135±3 (23.8%, p<0.001) mmHg after being subjected to bladder distension. The same results were obtained with respect to changes in systolic (155±2 mmHg) and diastolic (135±2 mmHg) blood pressure following bladder distension in animals with adrenal glands intact but with

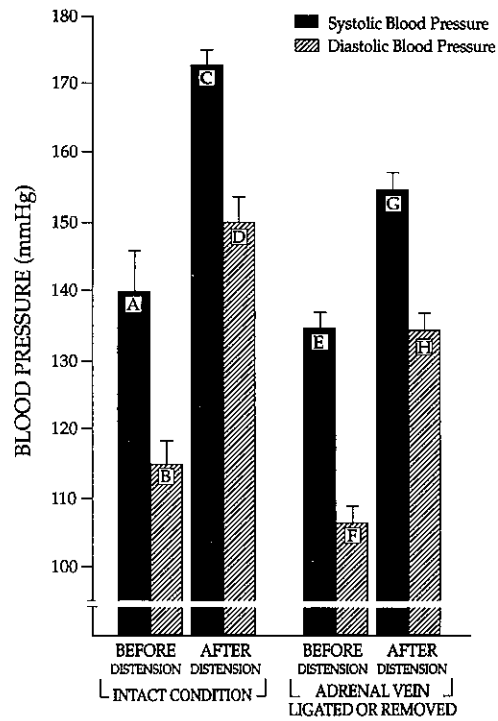

Fig. 3. Histogram illustrating the peak rise of blood pressure (systolic and diastolic) at 60 s of urinary bladder distension, before and after distension, in intact and adrenal vein-ligated or -removed condition. Columns A–H show the average±SEM (n=10) systolic and diastolic blood pressure changes at 60 s. The total distension was 90 s. The statistical analysis and comparison of all vertical bars is shown in Table 2.

Table 1. Relative contribution of adrenal gland function in intact/ligated/removed condition on viscerovasopressor response during urinary bladder distension (UBD).

	Systolic blood pressure			Diastolic blood pressure		
	Basal (mmHg)	After effect (mmHg)	% change	Basal (mmHg)	After effect (mmHg)	% change
Before UBD	140±5 (n=10)	—	—	115±3 (n=10)	—	—
After UBD (intact)	—	173±3 (n=10)	23.6%*	—	151±3 (n=10)	31.3%*
After adrenal vein ligated or removed (before UBD)	135±3 (n=10)	—	3.6%** (n=10)	109±3	—	5.2%**
After UBD ligated/removed	—	155±3 (n=10)	14.8%* 10.4%**	—	135±3 (n=10)	23.8%* 10.6%**

*Increased, **decreased. Basal values are mean±SE. n is the number of observations. The percentage change is calculated by: {(effect value−basal value)/(basal value)}×100=% change.

Table 2. Statistical comparison among the values of vertical bars A–H of Fig. 3.

In between	p value	t value
A & C	$p<0.0001$	−5.66
B & D	$p<0.0001$	−8.49
E & G	$p<0.001$	−4.71
F & H	$p<0.0001$	−6.13
A & E	$p<0.001$	4.24
B & F	$p<0.01$	3.77
C & G	Not significant p=0.4024	0.857
D & H	Not significant p=0.1744	1.41

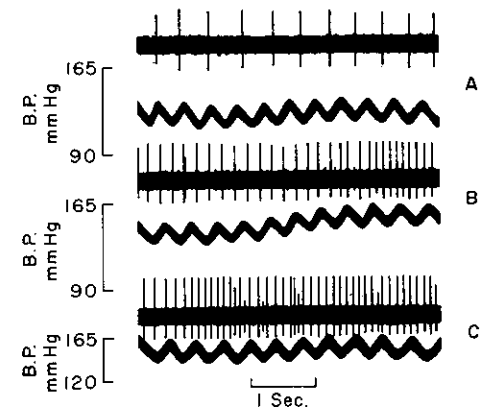

Fig. 4. The response pattern of spontaneous asynchronous efferent discharge from the adrenal sympathetic nerve (upper panel) with blood pressure (lower panel). Tracing A shows the resting discharge and B and C show the continuously increasing ($p<0.001$) firing of the single unit during urinary bladder distension with elevation of blood pressure.

bilateral ligated veins (Fig. 3, Tables 1, 2). The relative contribution of adrenal gland function in the intact/ligated/removed condition on viscerovasopressor response during urinary bladder distension (UBD) is shown in Table 1. The statistical comparison among the values of vertical bars in Fig. 3 is explained in Table 2. It appeared that adrenal glands had a direct influence on the viscerovascular reflexes.

Activity of adrenal sympathetic nerve during urinary bladder distension

The involvement of the adrenosympathetic nerve in altering the systematic blood pressure during bladder distension was studied by recording its single unit activity from the central cut end of this nerve. The spontaneous asynchronous resting firing rate was 1–3 spikes/s (Fig. 4A). The resting spike activity of the fibers was recorded before distension of the bladder. In reference to urinary bladder distension, an increase in activity ($p<0.001$) of the adrenosympathetic nerve along with the elevation of blood pressure was recorded over 90 s (i.e., the duration of the distension). The rate of electrical discharges was increased to 7–10 spikes/s during bladder distension (Fig. 4B, C). A total of 53 fibers were recorded from the adrenosympathetic efferent of the 17 cats. Of these, 46 units were active and 7 had no response (silent). It is evident, therefore, that the adrenosympathetic nerve was involved during bladder distension and the blood pressure increase was induced by sympathetic activity. Thus, like other sympathetic nerves, the adrenosym-

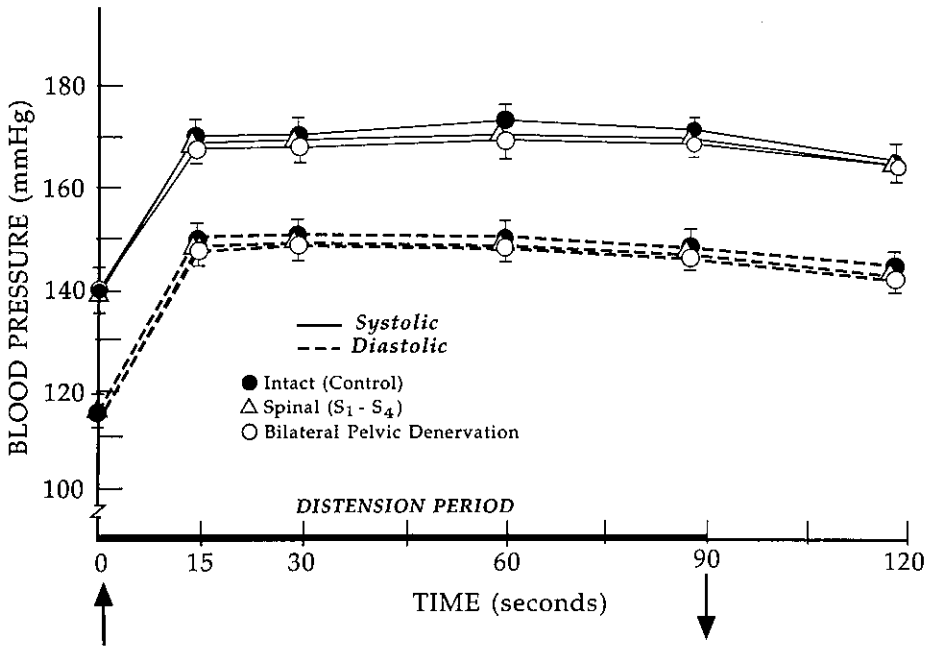

Fig. 5. Effect of urinary bladder distension on systolic and diastolic pressure in intact (control), spinal (S_1–S_4), and bilateral pelvic nerve-sectioned cat. Results are mean±SEM (n=10) and plotted against time. The total distension period is represented by arrows (↑↓).

pathetic nerve contributed to the enhancement of blood pressure during bladder distension.

Changes in blood pressure following bladder distension after spinal (S_1–S_4) transection and denervation of pelvic and hypogastric nerves

As usual, distension of the urinary bladder with warm, normal saline increased the blood pressure. It was found that spinal (S_1–S_4) transection as well as bilateral pelvic nerve denervation had no effect on the reflex rise of blood pressure caused by bladder distension (Fig. 5). The elevation of blood pressure was about the same in animals subjected to urinary bladder distension only and to both acute sacral dorsal rhizotomy and pelvic nerve denervation and distension. This result excludes the involvement of pelvic nerves (as well as parasympathetic nerves) in such vasopressor response.

Before denervation, the involvement of the hypogastric nerves in the rise of blood pressure during bladder distension was tested by local anaesthesia of the inferior mesenteric ganglion with Gesicain (2% lidocaine hydrochloride), when no vasopressor response took place during bladder distension possibly due to blockage of the transmission of impulses through the hypogastric nerve beyond the ganglion. Bilateral denervation of hypogastric nerves below the inferior mesenteric ganglion antagonized the usual blood pressure response to bladder distension and, consequently, there was no significant rise of blood pressure during bladder distension in hypogastric nerve-denervated animals (Fig. 5).

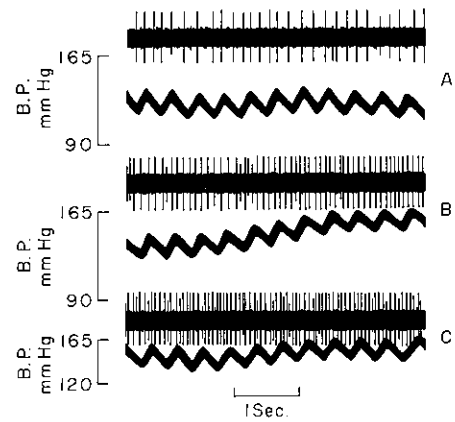

Fig. 6. The responsiveness of one spontaneous asynchronous afferent discharge of hypogastric sympathetic nerve (peripheral cut end) to bladder distension. "A" shows spontaneous activity (control). Tracings B and C show the increased discharge rate during the rise of blood pressure after distension. In all tracings (A–C) the upper panel represents neural activity and the lower panel represents blood pressure.

Activity of hypogastric nerve following distension of urinary bladder

The extremely rapid onset of blood pressure elevation during bladder distension implicated the active involvement of the nervous system and also implied spinal mediation of a reflex, involving afferent fibers rising within the bladder wall and ascending afferent pathway within the autonomic nervous system. Therefore, the single unit afferent activity from the peripheral end of the cut hypogastric nerve during bladder distension was recorded (Fig. 6). The resting rate of the electrical discharges from the hypogastric nerve

was found to be 4 to 6 spikes/s. Following distension of the urinary bladder (with innervation of the other side intact), the single unit activity of the hypogastric nerve was increased along with the rise of blood pressure. The firing rate was enhanced to 12–18 spikes/s during bladder distension (Fig. 6). It was thus indicated that the distension of urinary bladder caused a rise in blood pressure and the afferent pathways were running in the hypogastric nerves.

DISCUSSION

The involvement of the sympathetic nervous system for such visceral (viscerovasopressor) response was indicated earlier by Thomson and Witham [20] and Kurnick [21]. The vasopressor response to distension of the urinary bladder is presumably associated with increased sympathetic activity [7], since both this response with contraction of the nictitating membrane [22] and spleen [7] were significantly antagonized by α-blocker or ganglionic blocker [7]. It was also reported [22] that in reserpinized cats, distension of the bladder produced no vasopressor response, thereby indicating the involvement of catecholamines. The rise of blood pressure caused by bladder distension is undoubtedly due to vasoconstriction as well as peripheral sympathetic activation. We found in our previous study [7], that the spleen plays an important role in this reflex action due to bladder distension. However, the role of the adrenal gland itself by means of adrenosympathetic nerves in the viscerovasopressor response following bladder distension is still unknown. Hence, this study was designed to study the role of adrenosympathetic activity, as regards single fibers, in initiating cardiovascular changes during bladder distension.

The systemic blood pressure rose 23.6% (SBP) and 31.3% (DBP) due to bladder distension in intact animals. In this experiment, it was confirmed that phentolamine (2.5 mg/kg), guanethidine sulfate (20 mg/kg) and hexamethonium (1 mg/kg) completely antagonized the reflex response to bladder distension, whereas propranolol (β-blocker), at a dose of 2.5 mg/kg, did not counteract this response (Fig. 2). It is probable that distension of the urinary bladder reflexly stimulates the release of catecholamines (norepinephrine) from different peripheral sympathetic nerve terminals and also from other catecholamine stores (adrenal medulla) to produce peripheral vasoconstriction.

A similar suggestion was also put forward by Mukherjee [4] who reported that reflex vasopressor responses were probably due to splanchnic vasoconstriction. Our present study also demonstrates that the adrenal gland itself has a great influence in vasopressor response during bladder distension. The ability of adrenalectomy, or ligated adrenal veins, to modify by inhibiting (SBP: 10.4%, DBP: 10.6%) the response to bladder distension, indicates that it is mediated through the release of catecholamines from the adrenal glands (Fig. 3, Tables 1, 2). The catecholamines (epinephrine or norepinephrine), which are released from the adrenal medulla, act on the α-receptor and cause the splanchnic vessel to constrict. So, we confirmed that the hypertensive effect due to bladder distension was partly (SBP: 14.8%, DBP: 23.8%) due to sympathetic stimulation and partly (SBP: 10.4%, DBP: 10.6%) due to the release of catecholamines from the adrenal glands (Fig. 3, Tables 1, 2). After adrenalectomy, bladder distension still produced a vasopressor response, probably due to sympathetic ganglionic stimulation. This observation suggests that the adrenal glands are also likely to be directly involved, through catecholamine secretion along with other nervous structures, in the manifestation of such viscerovascular reflexes during distension of the urinary bladder.

The hypertension during bladder distension stimulates the carotid and aortic baroreceptors, producing reflex bradycardia (vagal effect) that overrides the direct cardioacceleratory effect of norepinephrine. Consequently, cardiac output per minute falls. Cats and some other species secrete mainly norepinephrine, but in dogs and humans, most of the catecholamine output into the adrenal vein is epinephrine [23]. It is known that adrenal medullary catecholamine epinephrine and norepinephrine act on α-receptors (excitatory effect), and β-receptors (inhibitory effect). The catecholamine that is secreted from the nerve endings also acts as an excitatory agent. Due to excitation, the systemic blood pressure rises due to vasoconstriction and the cardiac muscle excited; also, the smooth muscle of the spleen contracted [7]. The β-receptor has an inhibitory effect on blood pressure by vasodilatation and the use of a β-blocker did not prevent the viscerovasopressor response induced by urinary bladder distension.

To determine whether peripheral sympathetic activation due to bladder distension is the cause of this reflex rise of blood pressure during urinary bladder distension, the efferent sympathetic nerve from the adrenal gland was investigated. The adrenal glands are innervated from the greater splanchnic nerve. Fibers pass through the suprarenal plexus, pierce the surface of the gland, pass through the cortex and end in the medulla. They are medullated fibers without any cell station in their course and are entirely preganglionic. These nerves control the adrenal medulla only. They

are believed to have no action on the cortex [24]. The spontaneous asynchronous efferent single unit activities from the central cut end of the adrenosympathetic nerve with the rise of blood pressure during bladder distension was recorded. An increase in electrical activity of the adrenosympathetic nerve with the rise of blood pressure during bladder distension was observed. The resting firing rate from the adrenosympathetic nerve was significantly increased from 1–3 spikes/s to 7–10 spikes/s with the rise of blood pressure following bladder distension (Fig. 4 A–C). It appears that, therefore, that like other sympathetic nerves, adrenosympathetic nerves greatly contributed to the enhancement of blood pressure during bladder distension.

It was also found that spinal (S_1–S_4) transections as well as bilateral pelvic nerve (parasympathetic) denervation had no effect on the reflex rise of blood pressure caused by bladder distension (Fig. 5). Naturally, the rise of systolic and diastolic blood pressure was about the same in animals subjected to only urinary bladder distension, and to both spinal (S_1–S_4) transections and pelvic nerve denervation and distension. The afferent pathways for such reflexes are in the hypogastric nerve since such a response is absent after sectioning the hypogastric nerve. It remains unaltered after rhizotomy at the spinal S_1–S_4 levels.

The "intravesical threshold pressure" is the primary factor for the activation of afferent fibers. The reason for exclusion of the pelvic nerve afferent components are caused by lower intravesical threshold pressure for afferent activities in the pelvic nerve from the urinary bladder as compared with the hypogastric nerve. In our experiment, we produced pressure (30–40 mmHg) inside the bladder. This pressure, however, was not great enough to activate the pelvic nerve afferent. Therefore, if the pressure is increased to 70–80 mmHg, the bladder will develop nociception and activate the pelvic nerve afferent. It is also suggested that hypogastric and pelvic nerves mediate sensations of discomfort and pain from overdistension of the bladder. Although the bladder was not "overdistended" in our study, the intravesical threshold pressure probably caused intense afferent stimulation. Such intensity of afferent stimulation was required to cause significant sympathetic excitation and pressor responses. The exaggerated presence of vesicopressor responses in spinal animals suggests that this reflex is tonically suppresed by supraspinal influences [7]. Graded distension and contraction of hollow organs (colon, urinary bladder, gallbladder) lead to graded responses of the visceral afferent neurons. The stimulus-response relationships and distributions of intraluminal threshold pressure for the afferent units show that the thoraco-lumbar and sacral visceral afferents from hollow organs are largely homogeneous. No distinct population of high-threshold afferents which would qualify as "visceral nociceptive" could be separated from the whole population of spinal visceral afferents [25].

The functional characteristics of lumbar visceral afferent fibers from the urinary bladder and the urethra have been studied in the cat [26]. The afferent lumbar innervation of the urinary bladder and urethra is probably not essential for either continence (storage of urine) or micturition. Afferents with receptive fields on or in the bladder wall responded in a graded manner to passive distension and isovolumetric contraction at intravesical pressures ranging from about 10 to 70 mmHg. The thresholds for exciting the afferent units ranged from less than 10 mmHg to 30 mmHg intravesical pressure, most of them being less than 20 mmHg. Generally, the discharge rate of the afferent units gave a reliable representation of intravesical pressure to the lumbar spinal cord [26]. The afferent innervations of the urinary bladder and urethra in the cat have been studied and the nerve action potential recorded [27]. The activity of the sensory nerve endings of the urinary bladder and urethra has also been investigated [28]. The afferent fibers of the bladder are classified into two groups. The first group consists of the endings located outside of the bladder wall and are stimulated by the change in the position of the bladder or by pressure. Probably, these endings have no relation with micturition. The second group of endings are situated in the bladder wall. Some of these endings rapidly adapt and are stimulated by detrusor muscle contraction. Other endings slowly adapt and are stimulated by the increase in intravesical pressure. The threshold of the latter endings varies greatly and the frequency of discharge is enhanced with changes in intravesical pressure. These impulses from both groups of nerve endings travel through the hypogastric and pelvic visceral nerves.

It appears that the extremely rapid elevation of blood pressure during rapid bladder distension is possible only because of the active involvement and participation of the nervous system and it also implies spinal mediation of a reflex involving afferent fibers arising within the bladder wall and ascending afferent pathways within the autonomic nervous system. Further investigations were undertaken to record the single unit afferent activity from the peripheral end of the cut hypogastric nerve during bladder distension. The single unit activity of the hypogastric nerve was increased along with the rise of blood pressure follow-

ing bladder distension (Fig. 6). These results indicate that the reflex rise of blood pressure during bladder distension was affected by the increase in hypogastric nerve activity. It may be suggested also that distension-sensitive receptors in the bladder wall get activated during bladder distension with normal saline and send excitatory impulses through the hypogastric nerve to ultimately induce reflex hypertension. That these excitatory impulses do not pass through the pelvic nerve has been verified by rhizotomy at the S_1–S_4 level when there was no alteration in the reflex rise of blood pressure during bladder distension. These findings exclude the possibility of involvement of parasympathetic nerves in such viscerovasopressor response.

In conclusion, we found the partial inhibition of reflex hypertension during bladder distension after adrenalectomy. It is evident, therefore, that the adrenal glands (medulla) itself as well as adrenomedullary catecholamines, contribute to the rise of blood pressure. It is concluded that exclusion of the pelvic nerve (parasympathetic) involvement during bladder distension and also active involvement and participation of the adrenosympathetic nerve activity (partially) and catecholamine secretion, as regards single unit fiber activity, are documented possibilities the reflex viscerovascular responses. This evidence should provide significant additions to the understanding of the physiological and clinical importance of visceral (viscerovascular) reflexes, especially regarding cardiovascular abnormalities in paraplegic patients.

We gratefully acknowledge the financial assistance of the Indian Council of Medical Research and the Council of Scientific and Industrial Research, Government of India, New Delhi, India. We are also indebted to Professor H. Brunner and Dr. K. Sacheibli of Ciba-Geigy, Switzerland, for the generous gift of phentolamine mesylate. The authors wish to thank Mark Kern, Jody Bonnevier, Jan Staedler and Dr. Ravi Kambampati for their assistance in the preparation of this manuscript.

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