Chapter 8

Relationship Between Vesicular Movement and Urine Flow of Cardiac Origin
8.1. Introduction

In the patients with coronary heart diseases (CHD) like myocardial infarction, frequent urination and defecation are some of the most important visceral symptoms. In normal human and animals, the primary stimulus for the micturition reflex is the urine storage and consequent distension of the urinary bladder (deGroat, 1975). This storage of urine in the bladder and consequent distension of the same is naturally dependent on the diuretic function of the kidney. Although Vaughan and Satchell (1992) has shown that storage of urine remains inhibited during micturition reflex, there is no evidence that whether the process of urine formation in the kidney remains inhibited or not during micturition or increased vesicular pressure. In the previous chapters (Chapters 3 to 7) it has been elucidated that the stimulation of ventricular receptors by LAD occlusion or epicardial nicotine application evoked a biphasic response of the vesicular motility as well as the rate of urine formation. The vagus and sympathetic nerves apparently played important role in conveying the afferent impulse from the heart for the manifestation of these responses. So, in the present chapter, attempts have been made to elucidate whether there is any relationship between these two responses - the vesicular motility and the rate of urine formation, caused by the stimulation of the ventricular receptors.

8.2. Methods and Materials

8.2.1. Animal preparation and recording:

Experiments were carried out on 110 chloralose (60 mg/kg b.w) anaesthetised adult cats of either sex weighing 2-3 kg. The femoral vein was cannulated for intravenous administration of anaesthetics, different drugs and also 5% glucose saline (with 1M NaHCO₃ solution when required). The trachea was cannulated for giving artificial ventilation as and when required. The urinary bladder was cannulated via the urethra with the help of a polyethylene catheter. The cannula was connected to an INCO polygraph (Model No 201) through an INCO pressure transducer (Model No T301) via a three-way stopcock to record the bladder movement in terms of intravesicular pressure (IVP). In the record, the bladder contraction is reflected as increase of intravesicular pressure and relaxation of inhibition as decrease of intravesicular pressure (IVP). The ureters were cannulated by fine polyethylene catheters. One of the catheters was connected to a drop counter and urine drops were recorded as spike per drop on the INCO polygraph. Spikes per minute were counted to calculate the urine flow as drops/min. The left
chest was opened by removing 2nd to 6th left thoracic ribs keeping the animal under artificial ventilation. The heart was exposed by cutting the pericardium with a midline incision and a pericardial cradle was made with the ends of the cut pericardium. A small length of the left anterior descending coronary artery was cleared from the surrounding tissues and a fine silk thread was put around it. The artery was occluded reversibly for 3-4 mins. by pulling the snare giving an interval of 20 mins. between two successive occlusions. Nicotine (100-200 µg/ml) was applied for 30-60 secs. directly over the epicardial surface with the help of a fine cotton film of 7-9 mm diameter soaked with nicotine. The epicardial surface was washed with normal saline at least 4 times to remove all traces of nicotine from the surface and the next dose of nicotine was applied after at least 20 mins. Agonists and antagonists of different neurotransmitters were dissolved in physiological saline at a concentration so that the required dose was present in 0.5 ml and administered intravenously. Immediately after such administration, 0.5 ml saline was injected intravenously so that no drug remained within the cannula. For the preparation of animals with sectioning of vagi and cardiac sympathetic nerves, spinal cord and decerebration the methods described in chapter 2 under sections 2.2.9.1, 2.2.9.2, 2.2.12 and 2.2.13 have been followed respectively.

8.2.2. Drugs used:

Anesthetic ether (Kabra Drugs Ltd., India), α-chloralose (Koch-Light Lab, U.K.), Nicotine (C-) Nicotine, Merck-Schuchardt), Lignocaine ("Xylocaine", Astra-IDL Ltd., India), Atropine sulphate (Bengal Immunity, India), Phentolamine mesylate ("Regitine" Ciba-Geigy, U.K.), Atenolol ("Aten 25", Kopran Ltd., India), Salbutamol sulphate (Opec Innovations, India).

8.3. Results

8.3.1. Cardiac nociception, vesicular motility and urine flow:

LAD occlusion for 3-4 mins. evoked a biphasic response of both vesicular motility and urine flow. There was an initial large contraction of the urinary bladder and at the same time a decrease in urine flow rate (antidiuresis). After this, the vesicular movement was inhibited and urine flow rate was increased (Fig.8.1).
Fig. 8.1. Typical response pattern of the urinary bladder movement (upper tracings) and urine flow (lower tracings) in response to LAD occlusion (A) or epicardial nicotine application (B) in anaesthetised cats. Arrows indicate the duration of LAD occlusion or nicotine application.
Epicardial application of nicotine (100-200 μg/ml) for 30 secs. also evoked similar type of responses of the vesicular motility and the urine flow (Fig. 8.1).

8.3.2. Role of cardiac afferents:
Bilateral vagotomy partially but significantly counteracted (P<0.001) the initial large contraction but the initial antidiuresis remained unaffected. Rather, the late diuretic phase induced by coronary occlusion or epicardial nicotine application was completely abolished by vagotomy (Fig. 8.2).

Sectioning of inferior cardiac nerve (ICN) partially (P<0.05) counteracted the LAD occlusion or nicotine induced initial large contraction and completely abolished the inhibition phase of the bladder movement. On the otherhand, ICN sectioning abolished the initial antidiuretic phase only. The late diuretic phase remained unaltered (Fig. 8.2).

8.3.3. Role of spinal cord:
Spinal transection at the C7-C8 level completely abolished the spontaneous motility of the urinary bladder and also the reflex response of the bladder movement. Spinal transection decreased spontaneous urine flow rate. In such animals LAD occlusion or epicardial nicotine induced antidiuresis was unaltered but the diuretic phase was counteracted (Fig. 8.3).

8.3.4. Effect of decerebration:
Decerebration at the mildcollicular level abolished the initial large contraction of the cardiovesicular reflex and potentiated the inhibition phase. Decerebration reduced the spontaneous urine flow rate. But, the reflex biphasic changes of the urine flow was not altered (Fig. 8.4).

8.3.5. Effect of neurotransmitter blockers:
The initial large contraction and the inhibition of vesicular contraction were abolished by β2 and β1 adrenoreceptor antagonist respectively. But, the initial antidiuresis was counter-acted by atropine which had no effect on vesicular movement (Tables 3.2, 6.3). The diuretic phase was significantly counteracted by phentolamine which also had no effect on cardiovesicular reflex (Tables 3.2, 6.3).
Fig. 8.2. Typical response pattern of the urinary bladder motility (upper tracings) and urine flow (lower tracings) in control (A), bilateral vagotomised (B) and in inferior cardiac nerve (ICN) sectioned (C) animals. The arrows indicate the duration of nicotine application.
Fig. 8.3. Typical response pattern of the urinary bladder movement (upper tracings) and urine flow (lower tracings) in response to LAD occlusion in intact (A) and spinal (C7-C5) (B) animals. Arrows indicate the duration of LAD occlusion.
Fig. 8.4. Typical response pattern of the urinary bladder movement (upper tracings) and urine flow (lower tracings) in response to LAD occlusion in intact (A) and decerebrated (B) animals. Arrows indicate the duration of LAD occlusion.
8.4. Discussion

It has been observed that LAD occlusion or nicotine application caused biphasic responses in both vesicular movement and rate of urine formation (urine flow). Where the vesicular movement first rises and then declines, the rate of urine formation first declines and then increases. At this stage it seems likely that the two individual events coincides, i.e., the increased intravesicular pressure (IVP) coincides with the fall of the rate of urine formation and vice-versa. To be sure about this, further experiments were carried out after the cardiac nerves sectioning, spinal and supraspinal lesioning and also by blocking the sensory receptors with specific blockers.

From the experiments of afferent cardiac nerve sectioning, it is clear that, the afferent limbs for the two superimposed events are different. While vagus sectioning partially counteracted the initial large contraction, ICN sectioning completely abolished the initial antidiuretic phase. Similarly, while ICN sectioning partially counteracted the initial large contraction of the vesicular response and completely abolished the late inhibition phase, the late diuretic phase was completely abolished by vagotomy. Thus, in partial absence of the initial large contraction in vagotomised animals, the initial antidiuresis was still present, rather, the late diuretic phase was abolished. So, the initial antidiuretic phase was not dependent upon the intravesicular pressure rise. Similarly, the diuretic phase was also not dependent on the inhibition of vesicular contraction.

In spinal animals at the level of C7-C8, the vesicular motility - both spontaneous and reflex, were completely absent. But, at the same time, the initial reflex antidiuresis was present although the late diuresis was absent. Thus, in spinal animals, the antidiuresis was present without the simultaneous reflex large contraction of the urinary bladder.

Further, in the decerebrated animals, the initial large contraction of the reflex vesicular movement was absent. At the same time, the reflex antidiuresis was present. So, again it is seen that the two superimposed events are not dependent on each other.

Finally, the neurotransmitters involved in such responses are completely different, Atropine, which was totally ineffective in the manifestation of the reflex vesicular motility, counteracted the initial antidiuresis. Thus, in presence of initial large contraction of the vesicular movement, the
antidiuresis was prevented.

From all these observations, it is now clear that, although in the intact control cats, the biphasic changes of the vesicular motility and rate of urine formation (urine flow rate) were superimposed, these are not interdependent. The subsequent experimental results clearly showed that the initial antidiuresis can take place even in absence of initial large contraction of the vesicular motility, i.e., when the intravesicular pressure rises. Thus the increased IVP plays no significant role in inhibiting the urine formation rate by the kidney. Similarly, it has also been observed that, the inhibition of bladder contraction had no effect on increased rate of urine formation (diuresis).

So, it can be opined that the reflex changes of vesicular motility and the reflex changes of urine formation are not dependent on each other, rather these are two separate reflex effects in response to ventricular receptor stimulation.