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CHAPTER 7

A STUDY OF THE URETERIC PERISTALSIS USING A SINGLE CATHETER TO RECORD EMG, IMPEDENCE AND PRESSURE CHANGES

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ABSTRACT

Introduction: Ureteric peristalsis transports a urinary bolus from the renal pelvis to the bladder. We developed an intraluminal catheter with a pressure transducer on it to study intraluminal pressure changes and a twin bipolar electrode records the ureteric EMG and impedance (Z) changes during a peristaltic wave.

Material and methods: Five female New Yorkshire pigs (50-60 kg) were studied under light halothane anesthesia (5% at induction/ 1% for maintenance). A steady state of hydration was maintained using intravenous saline infusion. EMG spike burst activity was studied at a 10 cm interval using low (0-30) Hz filters. Impedance between the same electrodes is measured simultaneously in higher frequencies (1-5 KHz) as a function of ureteric motor activity. Pressure generation in the ureteric lumen was also measured simultaneously by a transducer on the same catheter. A digital signal-processing program (Poly® 4.9) was used for analysis. Parental Furosemide was used to induce diuresis.

Results: Resting ureteric impedance ($Z_R$) decreases to $Z_B$ ($Z$ bolus) during the passage of the urinary bolus. Passage of a contractile zone during a peristaltic wave increases impedance from $Z_B$ to its $Z_R$ level and initiates a pressure rise. Bolus length (the length $Z_B$) is not constant and decreases distally. EMG corresponds in time to impedance well. $Z_R$ disappears after infusion of Furosemide because of increased urine load and changes of intraluminal ionic environment. Contractile segment of a ureteric peristaltic wave appears to be represented by an elevated $Z$ segment ($Z_C$). Pressure rise is recorded only at the beginning of a contractile zone.

Conclusions: A specially adapted intraluminal catheter can be used to study peristalsis in the upper urinary tract. One can study all the three components of ureteric peristalsis (excitation, contraction and intraluminal pressure rise) using such a catheter.
INTRODUCTION
Urine is transported through the ureter into the bladder by periodic peristaltic activity. Griffiths and Notscheale\(^1\) have described that ureteric peristalsis transports urine from the renal pelvis in the form of isolated urinary boluses. When diuresis increases, these separate boluses first touch each other to form “kissing boluses” and then merge into adjacent ones to finally form an “open tube flow”. Urinary transport is essentially unidirectional. From our morphological and dynamic studies in the distal ureter at the ureterovesical junction, we have evolved a dynamic hypothesis of peristalsis as an active anti-reflux mechanism at the juxtavesical level. The current study was part of this larger project\(^2\).

In the current article, we discuss our method of studying ureteric contraction by using the variation of impedance, the ureteric EMG activity and endoluminal pressure rise simultaneously by using a single endoluminal catheter. The importance of this technique is that it can be used in an experimental setting to study pharmaco-neuromodulation of ureteric peristaltic activity in a chronically instrumented animal. The modulation of ureteric motility by pharmacological agents has an obvious potential therapeutic use for the treatment of motility disorders of the upper tract.

MATERIAL AND METHODS
Experimental animals and the anesthetic procedure. Five New York-shire female pigs (n=5, 57±7 kg) were studied. Anesthesia was controlled to maintain optimal muscular activity during the experiment. Twenty mg Azaperon and 150 mg Ketamine per 10 kg body weight and 1 mg Atropine were administered as pre-medication prior to general anesthesia. General anesthesia was induced by using 5% Halothane and maintained by 1% Halothane and a mixture of each 50% N2O and O2. Antibiotic cover (1200 mg Augmentine) was employed during the study. Hydration was maintained by infusing 0.35±0.08 L/hour of physiologic saline solution. This infusion rate was chosen because the animal was fasting for more than 12 hours preoperatively and general anesthesia produces a blood pressure drop. To deal with these problems in order to keep an optimal circulation that infusion rate was needed. Urine produced was macroscopically not diluted. Continuous monitoring of blood pressure, electrocardiographic and pulmonographic parameters was maintained during the whole procedure to ensure optimal metabolic functioning. Furosemide and more fluid were used to study the effect of increased diuresis on ureteric motor activity.
Analgesics and postoperative antibiotic cover were employed for the comfort of the animals.

*Electromyographic/impedance/pressure measuring catheter* (Fig. 1). EMG complexes and impedance variation were obtained endoluminally using two bipolar ring electrodes fixed to an especially designed 6F ureteric catheter at a distance of 10 cm from each other. A piezo-electric crystal was attached adjacent to the ring electrodes to measure pressure rises in the ureteric lumen.

**Figure 1:** schematic representation of our measurement catheter. Pressure sensitive pizo-electric crystal registers pressure alterations. Two ring electrodes adjacent to these crystals registers the EMG at lower frequencies and Z at higher frequencies.

This catheter could be introduced through a working channel of a 22F rigid cystoscope. We recorded the ureteric electrical activity at 3 and 13 cm from the ureteric orifice. The indifferent electrode was connected to the cystoscope. The other working channel of the cystoscope was used to ensure that the bladder remained empty during the recordings. EMG was recorded using 0-30 Hz pre-amplifying filters. A sampling frequency of 100 Hz was established according to the Nyquist principle. The resting impedance ($Z_R$) was approximately 4 KΩ using a 500 Hz AC generator. The impedance signal was filtered at 1-5 KHz. The Pathfinder II Nicollet® was used as an amplifier. An analog/digital interface (DAS-8-PGA, Keithley Instruments, Cleveland, OH, USA) with 12-bit resolution was used to digitize the signal. Digital signal processing was undertaken using Poly 4.9, a digital signal-processing program running on a 586-100 MHz IBM compatible computer.
RESULTS

Ureteric peristalsis during normal diuresis. Resting impedance of the ureter (Z_R) decreases during the passage of urinary bolus to Z bolus (Z_B, Fig. 2). This phenomenon can be explained by the fact that resistance (Z) decreases in an ionic environment, which is constituted by a urinary bolus. Passage of the contractile zone of peristalsis increases Z to Z contraction (Z_C), which almost equals Z_R level and initiates the pressure wave (Fig. 2).

During the passage of the contractile zone, the ionic fluid bolus of urine is squeezed away from the two electrodes and therefore the resistance (Z) is increased. Bolus length (e.g. the length of Z_B) is not constant at a particular ureteric level and also decreases distally in the ureter (Fig. 2). EMG corresponds in time to the beginning of Z_B. EMG signal diminishes temporarily during a passage of urinary (Fig. 2).

Ureteric peristalsis during increased diuresis. Z_R decreases and even disappears during Furosemide induced state of diuresis probably due to greater disturbances of the ionic environment (Fig. 3). Contractile segment of the ureteric peristaltic wave is represented by a broader Z_C segment (Fig. 3). The fact that the constricted segment of the ureter is longer distally in the

Figure 2: EMG/ impedance/ pressure change during the passage of a separate urinary bolus during a normo-diuretic state. Note that the Z_B is shorter in the distal part of the ureter.
ureter supports the idea that the peristalsis in the distal ureter can act as an active anti-reflux mechanism as postulated by us. Intraluminal pressure rise is seen only at the beginning of a contractile zone (Fig. 2 and 3).

**Figure 3:** EMG/impedance/pressure change during the passage of a contraction wave over a ureter in its open tube state. Pig was prescribed 60 mg furosemide and 500 ml physiological saline solution.

**DISCUSSION**

Ureteric peristalsis is a sequence of excitation of the muscular components (EMG activity), their contraction (constriction where circular muscle bundles are present) and the segmental rise of ureteric wall tension in order to generate a peristaltic movement (Fig. 4). The length (velocity of signal conduction differentiated in time) and the duration of the EMG active zone in the distal ureter indicate respectively the length of a “constricted” ureteric portion and the duration of its contraction. They are valid parameters of ureteric peristalsis and help to occlude the ureter temporarily, thus guaranteeing a unidirectional fluid transport and preventing retrograde leakage of intraluminal fluid in the upper urinary tract.
The ureteric EMG and manometry have been studied separately and published by several authors\textsuperscript{3-10}. Ureteric contraction has been studied using different methods varying from video-microscopic imaging technique\textsuperscript{11}, color doppler\textsuperscript{12}, the ultrasound\textsuperscript{13}, cineradiography\textsuperscript{14} and 99Tcm-MAG 3 radio nuclide condensed imaging\textsuperscript{15}. The major problem in these reported studies is the fact that different techniques and instruments were employed to study the different components of peristalsis. Also multiple instrumentations and experimental sessions were necessary. The procedure are thus not only labor intensive, but also may affect negatively the normal upper tract physiology since multiple instrumentation is often described. We could not find any report in the literature from Med. line search (1963-1997) in which an author had studied the 3 components of the ureteric peristalsis simultaneously.

![Figure 4: The sequence of Excitation, Contraction and the pressure rise within the ureter. Asterisk (*) represents the pacemaker cell in the muscular wall of the renal pelvis and calyces.](image)

\textit{Upper urinary tract urodynamics, data acquisition and technical consideration.} Data acquisition is a major problem in the case of the upper urinary tract urodynamics. Urodynamics of the upper urinary tract has been less intensively studied. Reliable data from a minimally invasive technique to study the upper urinary tract at standard locations has not been possible until now. The absence of standard values for the for-said physiological parameters at the upper urinary tract also adds to difficulty in communication between different groups of investigators.

Simultaneously recording of EMG, ureteric wall movement and, or intraureteric pressure rise deliver usefully information concerning the coupling of the excitation and the contraction cycle. It is however not easy to
acquire reliable data on ureteric movement. Imaging techniques using X-ray contrast agents and old-fashioned roentgen-cinematography provided only momentary visualization and not a real time imaging. Implantation of movement detectors on the ureter requires surgical intervention, which affects the ureteric physiology. The use of color Doppler ultrasound as described by Summers et al\textsuperscript{17} and later by Patel U.\textsuperscript{12} may be a new useful non-invasive technique. However all these techniques require multiple handling of tissue and are difficult to combine with simultaneous EMG and manometric study of upper tract dynamics.

Our preliminary results obtained by using a single catheter are promising. We were able to study all the three aspects (excitation, contraction, pressure rise) of the ureteric peristalsis, using minimal invasive technique. The catheter is so designed that it can be used ante-gradely through a percutaneously nephrostomy in chronic instrumented animal studies in vivo. The influence of different pharmacological agents on ureteric physiology in a chronic instrumented animal is being currently investigated by our group.

*Upper urinary tract urodynamics, characteristics of peristalsis.* Griffiths and Notscheale\textsuperscript{1} have described how ureteric peristalsis transports urine from the renal pelvis in the form of isolated urinary boluses. When diuresis increases, the separate boluses touch each other to form “kissing boluses” and then merge into adjacent ones to finally form an open tube flow.

Fig. 2 shows the characteristics of an isolated bolus. The drop of the $Z_R$ to the $Z_B$ level and the EMG signal indicate the arrival of a urinary bolus. The length of the narrow Z-segments ($Z_B$) depends on a, the volume of the urinary bolus (e.g. bigger the bolus, longer the narrow segment $Z_B$) and b, the compliance of the ureter segment (more compliant the ureter, shorter the narrow segment and higher the diameter of the bolus). Bolus length (e.g. the length of $Z_B$) is not constant at a particular ureteric level (bolus volume changes) and also it decrease distally (compliance decrease distally). This finding is also supported by the cinematographic study of Durben G. et al\textsuperscript{14} and the histological study of Knudsen L. et al\textsuperscript{18}.

Fig. 3 demonstrates the situation when diuresis is increased as results of using a diuretic agent and the boluses are merging to each other. Our experimental technique confirms the urodynamics occurring as postulated in Griffiths's model\textsuperscript{1}. The $Z_R$ narrowed and finally disappeared because of an overload of the ionic intraluminal environment and thus a lower electrical resistance. The contracting segments of peristalsis squeezes the
ionic fluid away only for a short time and thus is able to increase the Z to \( Z_C \) temporarily. In the diuretic phase condition, the amount of the \( Z_C \) is clearly seen. The longer lasting and trapezium shaped constricting effect of contraction in distal ureter at the level of UVJ in comparison to mid ureter (rectangular shape) supports our hypothesis concerning an active valvular function for the UVJ\(^2\). The findings of Knudsen L. et al\(^{18}\) that the distal ureter is also less compliant to form changes and passively resists relaxation would also concurs with our hypothesis.

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