The Influence of Internal Drainage of the Upper Urinary Tract on Urodynamics and Ureter Contractile Function

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S-shaped catheter-stents, when introduced in the upper urinary tract (UUT), facilitate the removal of stones from the kidney and ureter during endoscopic procedures and extracorporeal lithotripsy [4-6]. The stents are effective in preventing and liquidating a UUT obstruction and associated complications. However, undesirable consequences of internal drainage of the UUT, such as chronic inflammations and hypertrophy of the smooth muscle wall, have also been described, especially in the long term [3,7]. The purpose of the present work was to study the consequences of UUT internal drainage by stents with respect to UUT urodynamics and the contractile function of the ureteric wall.

MATERIAL AND METHODS

Experiments were carried out on adult dogs of both sexes weighing 20-28 kg and having intact UUT. The direct reaction to stent installation in the intact UUT was studied in five dogs. The period of S-stent application varied in 10 ureters (9 dogs): 1-2 weeks in two dogs, 1 month in six dogs, and 11 months in one dog. The state of the UUT was assessed immediately after stent removal and three and six months later.

The function of the kidneys and UUT was assessed by the routine X-ray and radioisotope methods. Diuresis and creatinine clearance were determined. The dynamics of the intraureteric pressure and the bioelectric and peristaltic activity of the UUT wall were studied by electroureterography (EUG) and impedance ureterography (IUG) [2]. Contractile function of the smooth-muscle wall was judged from contractions in isolated segments cut out of the UUT and placed in a special experimental *in vitro* device [1]. Morphological control was also performed by light and electron microscopy.

RESULTS

The direct introduction of a catheter-stent into the UUT caused an increase of the bioelectric activity of the wall and suppression of the peristaltic amplitude, these parameters depending upon the stent diameter. For introduction of catheters №5 and №9 (after Sharrier), peristalsis amplitude decreased by 23% and 81%, respectively, this also being accompanied by arrhythmia, a decrease of contractile frequency, or a constant excitation of the ureteric wall in the form of continuous peaks of diverse amplitude of the electroureterogram (EUG) and impedance ureterogram (IUG) records (Fig. 1).

Moderate UUT dilatation was observed in practically all the dogs after catheter-stents were intro-

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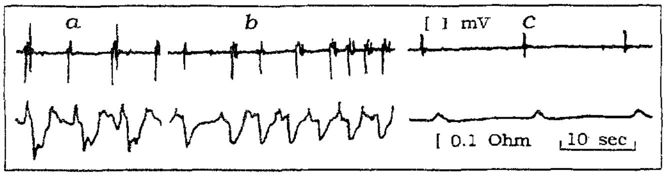

Fig. 1. Examples of electroureterogram recordings (top curve) and impedance ureterogram (bottom curve) in dogs during ureter drainage by catheter: *a*) thin, № 3 after Sharrier; *b*) № 5 after Sharrier; *c*) thick, № 9 after Sharrier.

duced. A bladder-ureter reflux was discovered roentgenologically and urodynamically. An insignificant UUT dilatation and ureter contrasting along its whole length were preserved long after stent removal.

No disturbances of ^{131}I-hippuran secretion by the renal tubules were found during the radioisotope studies of the function of the kidneys and UUT a month after the catheter-stents were introduced. However, a moderate slowing of evacuation or its reflux was observed.

Creatinine clearance in the dogs after stent removal accounted on average for 12.1±4.2 mmole/liter (16.5±2.5 mmole/liter in intact dogs).

The urodynamic parameters in the dogs one month after UUT drainage are presented in Table 1. A moderate increase, during the phases of both ureter relaxation and peristaltic wave passage, of the intraureteric pressure and a decrease of peristaltic frequency were observed in the functionally resting state immediately after stent removal.

The multichannel record of the contractile and bioelectric activity of the ureteric wall showed the presence of ectopic foci of spontaneous contractions induced by the stents; antiperistaltic waves arose periodically in different parts of the ureter (Fig. 2).

Refluxing peristalsis in the ureter after its drainage by a stent was probably the cause of the observed increase of the intraureteric pressure and led to the development of nephrohydrosis, discovered during the morphological investigation of biopsied kidney tissue. The degree of nephrohydrosis depended upon the duration of UUT drainage by stents.

A less marked increase of the ureteric pressure vis-a-vis the control was observed during the functional diuretic test (intravenous injection of lasix) performed after stent removal, as well as a smaller increase of peristalsis frequency (Fig. 3). The reaction to the diuretic test in the group of dogs in which UUT was drained by stents was specific, a bolus character of peristalsis being preserved under forced diuresis: pressure fluctuations of peristalsis were observed in 63% of the dogs of the experimental group. On the contrary, the urine flow along the ureter after lasix injection became continuous, showing no pressure increases of peristalsis in most observations (63%) in the control group of animals. A less marked rise of the intraureteric pressure and a slight increase of the frequency of bioelectric activity were also registered during the loading perfusion test (warm physiological saline pumping with a volume flow rate in the range of 1.8-13.0 ml/min). The values of ureteric resistance, calculated as the ureteric

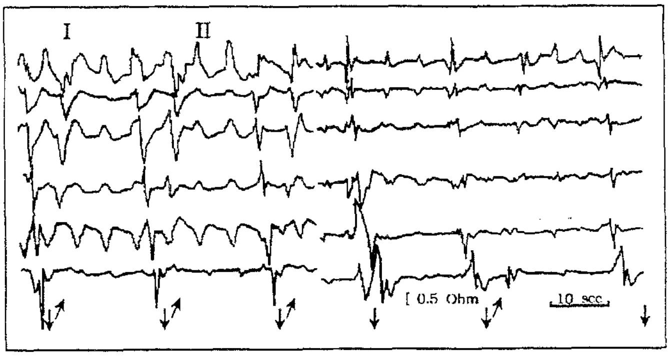

Fig. 2. Examples of simultaneous multichannel recordings of impedance ureterogram in a dog six months after internal drainage of ureter. 1) recording from upper part of ureter; 2) recording after multicontact electrode was moved to lower part of ureter. Peristalsis direction shown by arrows below.

pressure divided by the flow rate of perfusion, fell in both the diuretic and perfusion tests after UUT drainage was performed.

A significant decrease of ureteric contractile ability (maximal contractile force normalized for the thickness of segments) was observed during *in vitro* physiological studies of the upper third of ureters after their drainage (Table 2), their average weight and length being elevated in comparison to those of

TABLE 1. Urodynamic Indications of Dog Upper Urinary Tract after Its Drainage by S-Stents during One Month (1) vis-a-vis Control Animals (2)

Diuresis, ml/min	Pressure in ureter		Impedance ureterography amplitude, Ohm
	basic/peristaltic, cm water column	frequency, oscillations per min	
(1) 0.5±0.1	13±2*/30±9*	9±3*	1.46±0.43
n=6	9/8	6	15
(2) 0.4±0.3	8±1/22±3	16±1	1.66±0.52
n=13	36/26	27	16

Note: *: $p<0.05$

TABLE 2. Physiological Characteristics of Dog Ureter Fragments in the Norm and after Introduction of S-Stents (Contracting *in vitro* in Locke's Solution at 37°C)

Parameter	Unchanged ureters		After S-stents	
Weight, mg	24±3	(39)	89±12*	(19)
Length, mm	6.3±0.5	(39)	8.0±0.6	(19)
Resting tension, mN	2.99±0.7	(36)	4.48±0.9	(19)
Maximum isometric tension induced by rhythmic electric stimulation, 6 pulses per min	3.53±0.61	(37)	1.06±0.35*	(19)
Maximum isometric tension after resting, mN/mm	3.88±0.68	(37)	0.98±0.28*	(17)
Tension of hyperpotassium contracture, mN/mm	1.89±0.33	(33)	1.76±0.42	(18)
Percentage change of contractile force after isadrine	55±12%	(10)	107±11%*	(4)
Percentage change of contractile force after phentolamine	84±8%	(10)	124±14%*	(9)
Percentage change of contractile force by isadrine after phentolamine	62±14%	(8)	134±18%*	(4)

Note: *: $p<0.05$

the intact UUT. At the same time the potassium contractile tension determined in the segments did not differ significantly from that measured in the unchanged ureters. The adrenergic regulation of contractile function changed in the ureteric segments: the stimulation of β-adrenoreceptors with isadrine against the background of α-adrenoreceptor blocking with phentolamine had a positive inotropic effect, whereas stimulation of the β-adrenoreceptors of the intact UUT induced suppression of contractile function [1]. Such results attest to a qualitatively different state of the cells in the smooth muscle of UUT after stents had been introduced into them. The specificity of the reactions to the loading tests can probably be explained, to a certain degree, by the changes of humoral regulation in the smooth muscle wall found *in vitro*.

The results of the functional investigations were verified by the morphological observations: signs of an increase of leiomyocyte functional activity were found shortly after the stent had been introduced into the ureter. After the ureters had been catheterized for a month or more, transformation of leiomyocytes into myofibroblasts and growth of collagen fibers in the basal membrane of the leiomyocytes were observed.

When the ureter was drained during 11 months, more obvious disturbances of urodynamics were observed: peristalsis amplitude was reduced and disturbed by frequent retrograde waves; there was a decrease of ^{131}I-hippuran secretion by the renal tubules and morphological signs of wrinkling were found in the kidneys.

Thus, functional changes of the UUT and morphological manifestations of renal and ureteric dysfunction are caused by stents introduced into the ureter. The acute reaction consists of hyperexcitation and activation of contractile function. This is followed by contractile discoordination developing in different parts of the ureter, evoking refluxes and an increase of pressure in the UUT. The humoral regulation of the ureter contractile function changes on the cellular level. The positive clinical effect of stents in patients with UUT stones can be attributed to the observed decrease of the resistance to urine flow and an activation of wall contractility

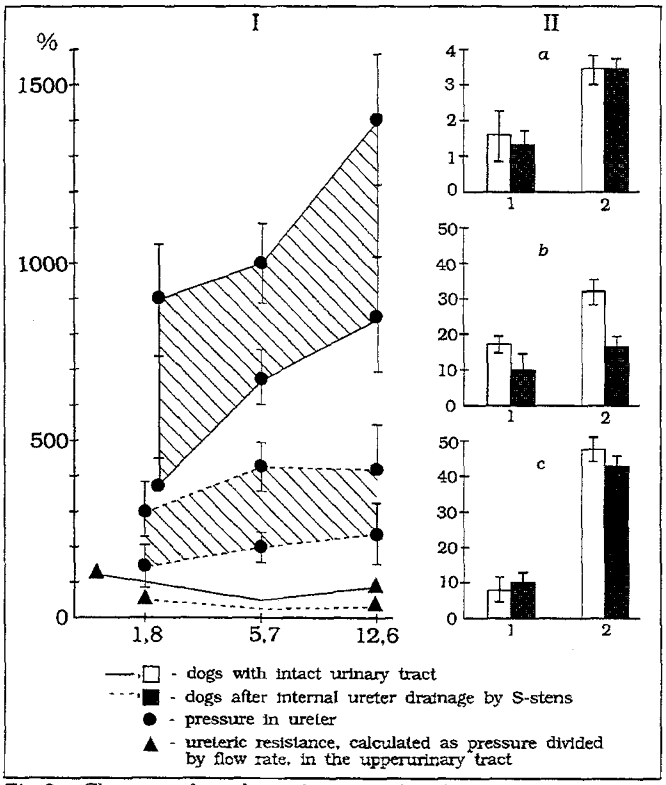

Fig.3. Changes of urodynamic parameters in upper urinary tract during loading tests. I) perfusion; II) diuretic test in dogs with intact urinary tract, and in dogs after internal ureter drainage by S-stents. Abscissa: changes (%); ordinate: volume flow rate of perfusion fluid along ureter, ml/min. Interval between basal and peristaltic values darkened. The following values are represented as columns: *a*) peristalsis amplitude according to impedance ureterography; *b*) peristalsis frequency; *c*) intraureteric pressure; 1) initial values, 2) after injection of lasix.

against the background of forced diuresis. Nevertheless, the results raise the problem of the advisability of prolonged UUT drainage and underline the necessity of pathogenic indications for the clinical choice of periods of stent use.

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Endogenous Intoxication Syndrome in Patients in the Late Stages of Obliterating Atherosclerosis of the Vessels

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The role of the main disease in the development of endogenous intoxication syndrome and the relationship of the latter to the stage of atherosclerosis have not yet been clarified. The urgency of this problem stems from the fact that the progression of vessel injuries and the complications sometimes accompanying surgical treatment may provoke the development of acute endotoxicosis [6].

Therefore, the goal of this work was a study of the component contents of the plasma in the context of the pathogenesis of atherosclerosis and endogenous intoxication syndrome in patients with obliterating atherosclerosis of the lower extremities (OALE) at various stages of lower extremity ischemia.

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A number of processes, such as lipid peroxidation (LPO), alterations in the peptide composition of the plasma, immunopathogenic reactions, and insufficiency of the detoxication system, are known to play an important role both in the pathogenesis of atherosclerosis [5] and in the development of endogenous intoxication syndrome [9]. These factors were decisive in the choice of the biochemical and immunological methods used in this study.

MATERIALS AND METHODS

One hundred five OALE patients aged 41 to 72 years were examined. The patients were divided into two groups. Group 1 included 61 patients with stage III ischemia of the lower extremities, according to Pokrovskii's classification [11]. The patients had an average age of 47 years, with a 4.9-year mean interval

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