

ASSESSMENT OF URODYNAMIC BLADDER BEHAVIOR ON FILLING WITH SOLUTIONS REPRESENTING PHYSIOLOGICAL EXTREMES OF URINARY OSMOLARITY

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ABSTRACT

Objective: Verify if there is any difference in sensitive and motor bladder response in the presence of solutions with different osmolarities, simulating physiological extremes of urinary osmolarity.

Materials and Methods: Thirty-three patients (24 men and 9 women) with mean age of 46.4 years (8 to 87 years) took part in this study. They were all subjected to 2 consecutive urodynamic examinations. In each exam, the vesical filling was accomplished by using a hyperosmolar (1000 mOsm/L) or hypo-osmolar (100 mOsm/L) sodium chloride solution in similar speed. The sequence in which each solution was instilled was determined by a double blind draw. The urodynamic results obtained from the infusion of both solutions were compared, regardless the sequence of administration.

Results: Fifteen patients (45.4%) showed detrusor hyperactivity, 12 of whom with neurological antecedents. The mean age of those with detrusor hyperactivity was 45.8 years, against 46.9 for those without hyperactivity. The infusion of the hyperosmolar/hypo-osmolar solution generated the following results, when comparing patients without vs. with detrusor hyperactivity: initial sensation of vesical filling (mL): 167.5 / 159.2 vs. 134.9 / 157.3 ($p > 0.05$); volume of occurrence of the first involuntary bladder contraction (mL): 163.9 / 151.9 ($p > 0.05$); detrusor micturition pressure (cm H₂O): 24.0 / 24.4 vs. 13.8 / 27.5 ($p > 0.05$).

Conclusion: The vesical filling with solutions simulating extreme urinary osmolarities, accomplished with similar speed and without previous identification, did not likewise alter the sensitive and motor urodynamic behavior in the current study.

Key words: bladder; urodynamics; hypertonic solutions; hypotonic solutions; overactive bladder
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INTRODUCTION

There is no consensus in the literature that factors such as pH and urinary osmolarity can contribute to bladder behavior variations and daily urinary pattern. Few are the works devoted to the study of vesical responses using solutions with different

physicochemical characteristics and their possible interactions with the urothelium. It has been demonstrated that solutions with alkaline pH have greater power of penetration through the cell membrane of the urothelium's apical cells (1). Other authors have verified that acid solutions instilled in the bladder during cystometry, triggered involuntary vesical con-

tractions in patients without previous vesical instability (2).

After studying the effects of urinary pH in bladder sensitivity in asymptomatic voluntary patients, we have concluded that the more acid the urine more precociously the sensation of vesical plenitude is manifested (3). There are still evidence of the occurrence of urinary osmolality variations and increase of sodium excretion in nocturnal diuresis in enuretic patients that can potentially relate the sensitive and motor cystometric behavior to change in bladder contents and osmolality (4).

The urothelium is the structure that keeps an intimate contact with the urine and its participation in bladder sensitive and motor response up to now is not completely defined. The classic concept of urothelial impermeability prevailed for decades, but has been questioned by many studies, such as the one that demonstrated a variation in urine composition from the renal pelvis to the bladder (5). This interaction between the urothelium and the urine can be explained by the transport of sodium that occurs through the apical cells, or yet, by the hypothetical existence of a counter-current mechanism, as the ones found in nephrons, conferring a larger participation of urine in the bladder functioning. (6). More recently, a synthesis of a substance by the urothelium was demonstrated, with an inhibitor role of the detrusor activity (7). Such a fact can correspond to at least one of the physiopathological processes responsible for the idiopathic detrusor hyperactivity, enuresis, and interstitial cystitis among other affections of the lower urinary tract.

The aim of this study is to verify if hyper- or hypo-osmolar solutions, representing the extreme of urinary osmolality, promote different responses in urodynamic parameters, when instilled inside the bladder during the cystometry.

MATERIALS AND METHODS

Sample

Thirty-three patients in an outpatient clinic follow-up took part in this study, all with indication of an urodynamic study performed as a subsidiary exam in the diagnostic investigation. This study was performed in patients with different ages, both sexes,

either with different bladder functional states and the presence or not of neuropathies (Table-1). By adopting this method, we tried to verify if some of these conditions could change the cystometric responses when performed with extreme osmolality solutions. Were excluded from this study patients that presented acute infection of the urinary tract, vesical neoplasia,

Table 1 – General characteristics of patients studied.

Initials	Age (years)	Sex	Primary Disease
VLSA	38	F	Diabetes mellitus
FP	38	M	Rachimedullar trauma (T6-7)**
AGC	77	M	Parkinson disease + HPB
INS	16	F	Transverse myelitis
ESA	14	F	Nocturnal enuresis
MAAP	29	F	Urinary urgency and incontinence
WRD	72	F	Urinary urgency and incontinence
NA	69	M	Lower urinary tract symptoms
VSG	22	M	Medullar dysraphia (S1)**
IMS	34	F	Effort related urinary incontinence
VM	39	F	Effort related urinary incontinence
MBB	66	M	Medullary vascular accident
MMMF	49	F	Effort related urinary incontinence
MCA	26	M	Rachimedullar trauma (C5-6)**
OOA	74	M	Prostatic hyperplasia
JCL	47	M	Lower urinary tract symptoms
VJT	50	M	Tropical espastic paraparesis
PPS	75	M	Vascular cerebral accident
VHS	26	M	Cervical and lumbar ependymoma
EPM	37	M	Rachimedullar trauma (T10)**
JFM	80	M	Vascular cerebral accident
GLL	49	M	Disk hernia
RAG	34	M	Rachimedullar trauma (T?)**
JASI	54	M	Rachimedullar trauma (L4)**
AFL	8	M	Vesico-ureteral reflux
EPLN	11	M	Repeated urinary infections
FS	87	M	Prostatic hyperplasia
JFC	61	M	Lower urinary tract symptoms
CN	73	M	Lower urinary tract symptoms
ATL	41	M	Rachimedullar trauma (T6)**
GLC	62	F	Effort related urinary incontinence
VAM	7	M	Cerebral palsy
RCO	68	M	Lower urinary tract symptoms

*M = male; F = female; ** Level of medullar lesion: C = cervical; T = thoracic; L = lumbar; S = sacral.*

stenosis of the urethra, in postoperative period of urinary tract or nervous system diseases in the last 2 months before the exam, patients in use of drugs that could interfere in the functioning of the vesico-sphincteric apparatus and presenting psychiatric disturbances.

All patients have received a detailed explanation of the procedure to be performed and an informed consent was signed. In the case of patients with less than 18 years old, the authorization for the performance of the exam was supplied by his/her legal representative. The study protocol was approved by the university's medical ethics commission.

To compare and analyze the results the patients were classified into 4 groups according to: a) age group, patients aged more than 40 and less than 40 years of age was defined as divisor, taking as a base the age median, by statistical approximation, thus constituting 2 similar subgroups, b) sex, male, female, c) presence or absence of detrusor hyperactivity: the criteria for the inclusion in each group was urodynamic. The patients that took part in the first group were those that presented presence of detrusor hyperactivity either in the first or in the second cystometry performed. The definition adopted for detrusor hyperactivity was the one established by the International Continence Society in 1988, i.e., the existence of detrusor contractions registered during the filling phase, that can be involuntary or provoked and that the patient is not able to suppress it completely (8). This was the detrusor hyperactivity definition in use in the beginning of the study. Those that did not fulfill such requirements took part on the group of patients without detrusor hyperactivity, d) bearers and non-bearers of neuropathies: were considered neuropaths the patients that presented any form or neurological disease, with potential repercussion for the urinary tract, already diagnosed or being investigated, independently from the primary etiology, time of evolution of the disease and intensity of the commitment, all the other ones were classified as non bearers of neuropathies.

Procedures

The osmolarities of the solutions were defined as 1000 mOsm for hypertonic or hyperosmolar and 100 mOsm for hypotonic or hypo-osmolar, being

those values close to the extremes possible to be found naturally in human urine (9).

The solutions were manipulated in the nephrology and the urology labs in our institution by means of a sodium chloride dissolution P.A. (Merck®) in distilled water. In order to reach the desired osmolarity, the quantity of solute necessary for such was calculated. Thus, the hyperosmolar solution, with 1000 mOsm, contained 528 mEq/L of sodium chloride that corresponded to the addition of 30.89 grams of the salt in one liter of distilled water. The hyposmolar solution, with 100 mOsm, contained 52.8 mEq/L of sodium chloride that corresponded to the addition of 3.089 grams of the salt in one liter of distilled water.

After the preparation, the solutions were distributed in the bottles and labeled as "solution A" or "solution B". The designation of a certain osmolarity was always the same. The biochemist responsible for the manipulation of the solutions denominated solution A, the hyperosmolar, and solution B, the hypo-osmolar. These denominations were kept secret until the end of the study.

The urodynamic exams were always performed by the same urologist. The urodynamic equipment used was Aquarius - Laborie® (Canada), with 3 channels for data obtainment and digital decoding of traced graphs. The urodynamic studies were only performed after the patient's physical exam, anamnesis and verification of subsidiary lab and radiologic exams.

Cystometry was performed with patients in the lithotomy position, in the conventional way using a double-channel urethral catheter 7F (Cook®), one for the liquid infusion, other for intravesical pressure registration and rectal balloon for simultaneous abdominal pressure registration. The solutions used in the cystometry were at room temperature and the speed of vesical filling was of 50 mL/min., controlled by an infusion pump.

Each patient was submitted to 2 sequential cystometries, each one with a hyper- or hypo-osmolar solution. It was a double-blind study. The sequence of the solutions to be instilled was defined by lottery, during each cystometry, in the first patient of this study. For the following patients the instilling

order was alternated (“quasi randomization”). In this way the sequence for patient 1 as solution A, for patient 2 solution B, in the second cystometry for patient 2, solution B in the first and solution A in the second and thus successively up to the last patient. The objective of alternating the solution sequence was to avoid being tendentious or having interferences between the 2 successive exams. Once the phase of vesical filling due to imperious desire to urinate or suprapubic pain referred by the patient was finished, a flow-pressure micturition study was performed. The patient assumed either orthostatic or sitting position and presented spontaneous micturition registered in the flowmeter. The ones that presented detrusor hyperactivity accompanied by involuntary urine loss before they could reach and keep a trustable vesical filling for registration (at least 150 mL), were not submitted to the flow-pressure study. The urethral catheter was kept in position and allowed the measurement of the final residual urinary volume. After a 5-minute interval to change solutions, the second cystometry was performed with the other solution.

The urodynamic parameters studied during the vesical filling were: volume and detrusor pressure at the moment that the initial sensation of vesical filling and the habitual micturition desire manifested, functional bladder capacity (maximum volume reached at the end of filling), pressure at the end of the vesical filling, volume in which involuntary bladder contractions occurred, the maximum pressure reached during these events and vesical complacency. In the comparative study between neuropathy bearers and non-bearers, vesical filling sensation variables were not assessed due to the error factor in interpreting these variables on the part of those patients with sphincteric neurogenic affection. In the phase of vesical voiding or urinary study the following urodynamic parameters: maximum urinary flow, mean urinary flow, detrusor pressure at the maximum flow, urinary volume and residual volume. All parameters studied are in consonance with metric units and definitions established by the International Continence Society.

Statistical Analysis

The results obtained for each urodynamic parameter studied in each group of patients were com-

pared according to the osmolality of the solution utilized and with the sequence of the exams performed (first or second exam). With this measurement, we could establish whether a difference in the results was due to an osmolar characteristic of the solution or whether it represented only a tendency result by the sequence of the 2 urodynamic studies. It was only considered of statistical significance the difference that occurred independently from the sequence of the instilled solutions.

In the statistical analysis of the results, the variables were submitted to logarithmic transformation aiming at stabilizing the variance (10). For the assessment of the means the multivariate method of analyzing mean profile, being fixed in 0.05 or 5% the rejection level of nullity hypothesis.

RESULTS

Basic Parameters of the Population Studied

The mean ages of the patients that participated in this study was 46.4 years and the median 47 years. Sixteen patients presented age inferior to 40 years and 17 patients more than 40 years, Twenty four patients were male with ages varying from 7 to 87 years (mean 49.2 years) and 9 female, with ages between 14 and 72 years (mean 39.2 years). Detrusor hyperactivity was found in 15 patients. The mean age of patients with detrusor hyperactivity was 45.8 years and of those without detrusor hyperactivity it was 46.9 years. Twelve bearers of detrusor hyperactivity were male and 3 were female. Neuropathy was present in 10 patients with detrusor hyperactivity and in 9 patients without hyperactivity. Only 2 patients did not present involuntary bladder contractions in the first cystometry and presented during the second. Both were male and the sequence of the instilling solutions was hypo-osmolar/ hyperosmolar for the first and hyperosmolar/hypo-osmolar for the second.

Comparison of the Hyper- and Hypo-osmolar Solutions According to the Parameters Studied

When the urodynamic studies obtained in the vesical filling and voiding are compared, to the hypo-

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and hyperosmolar solutions there was no statistical difference in the results in both age groups (Table-2).

No difference was found in any of the urodynamic parameters studied when exams utilizing hyper- and hypo-osmolar solutions are compared in female and male sexes (Table-3).

There was no significant difference in the cystometric and flow values in the presence of hyper-

and hypo-osmolar solutions, independently from the presence of detrusor hyperactivity or from the order in which the solutions were instilled. The volume in which involuntary bladder contractions occurred and the detrusor pressure reached during the same did not suffer any interference due to the intravesical osmolarity change. Aiming at minimizing error factors arising from the obtainment of only the group mean of

Table 2 – Values of urodynamic variables when vesical filling is accomplished with hyper- and hypo-osmolar solutions in patients with age inferior and superior to 40 years-old (mean ± standard deviation).

	< 40 years			> 40 years		
	N	Hyperosmolar	Hypo-osmolar	N	Hyperosmolar	Hypo-osmolar
Vesical filling phase						
Initial micturition sensation						
Volume (mL)	10	122.9 ± 72.1	111.0 ± 71.7	16	170.4 ± 148.1	178.6 ± 134.9
Pressure (cm H ₂ O)		4.3 ± 4.4	4.0 ± 4.9		4.4 ± 4.2	5.2 ± 4.8
Habitual micturition desire						
Volume (mL)	10	237.1 ± 144.9	213.1 ± 137.6	16	287.3 ± 238.9	293.6 ± 239.7
Pressure (cm H ₂ O)		14.6 ± 12.9	11.5 ± 9.9		10.8 ± 13.1	11.6 ± 10.8
Maximum bladder capacity						
Volume (mL)	15	268.1 ± 179.58	274.3 ± 179.4	18	366.3 ± 269.7	340.1 ± 252.6
Pressure (cm H ₂ O)		9.53 ± 13.93	9.5 ± 13.9		13.1 ± 13.1	11.2 ± 7.8
Complacency (mL/cmH ₂ O)	15	105.8 ± 130.8	110.1 ± 160.9	18	72.5 ± 97.0	59.3 ± 74.6
Involuntary bladder contraction						
Volume (mL)	7	145.6 ± 98.2	159.0 ± 127.1	6	185.3 ± 143.6	143.7 ± 105.3
Pressure (cm H ₂ O)		95.8 ± 35.5	85.3 ± 47.2		41.0 ± 22.1	51.8 ± 43.0
Vesical voiding phase						
Maximum flow (mL/s)	13	12.4 ± 11.6	12.0 ± 12.4	14	8.7 ± 4.7	9.6 ± 4.7
Mean flow (mL/s)	13	6.5 ± 6.4	7.0 ± 7.4	14	4.8 ± 3.1	5.3 ± 2.6
Detrusor pressure at the maximum flow (cm H ₂ O)	13	15.8 ± 15.9	20.4 ± 24.2	14	24.4 ± 27.4	29.2 ± 24.2
Micturition volume (mL)	13	178.8 ± 182.4	162.0 ± 194.6	14	205.8 ± 153.2	226.9 ± 167.9
Residual volume (mL)	13	93.2 ± 92.3	142.9 ± 151.7	14	222.1 ± 248.5	176.2 ± 216.4

* $p > 0.05$ for all variables in the comparison between hyper- and hypo-osmolar solutions and the sequence in which they were instilled.

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Table 3 – Values of urodynamic variables when vesical filling is accomplished with hyper- and hypo-osmolar solutions in female and male patients (mean ± standard deviation).

	Female			Male		
	N	Hyperosmolar	Hypo-osmolar	N	Hyperosmolar	Hypo-osmolar
Vesical filling phase						
Initial micturition sensation						
Volume (mL)	9	110.8 ± 83.5	109.6 ± 78.7	17	174.0 ± 139.3	175.4 ± 130.5
Pressure (cm H2O)		2.2 ± 1.6	3.67 ± 3.0		5.5 ± 4.7	5.3 ± 5.6
Habitual micturition desire						
Volume (mL)	9	187.4 ± 140.3	186.4 ± 134.3	17	310.6 ± 225.6	302.9 ± 230.2
Pressure (cm H2O)		11.2 ± 12.1	8.9 ± 8.9		12.8 ± 13.7	13.0 ± 10.9
Maximum bladder capacity						
Volume (mL)	9	261.7 ± 176.1	259.7 ± 153.6	24	344.2 ± 253.2	329.2 ± 242.3
Pressure (cmH2O)		5.56 ± 4.1	5.2 ± 4.2		13.7 ± 15.0	12.6 ± 11.6
Complacency (mL/cm H2O)	9	115.0 ± 148.5	80.6 ± 54.8	24	77.4 ± 98.4	83.0 ± 140.5
Involuntary bladder contraction						
Volume (mL)	3	127.3 ± 77.4	125.3 ± 83.1	10	174.9 ± 128.6	159.9 ± 123.2
Pressure (cm H2O)		82.0 ± 25.6	59.0 ± 50.2		67.1 ± 44.6	73.1 ± 48.0
Vesical voiding phase						
Maximum flow (mL/s)	7	18.3 ± 9.9	18.1 ± 10.4	20	7.7 ± 6.7	8.2 ± 7.3
Mean flow (mL/s)	7	9.9 ± 5.5	10.4 ± 6.5	20	4.1 ± 3.8	4.7 ± 4.3
Detrusor pressure at the maximum flux (cm H2O)	7	18.7 ± 11.9	28.0 ± 27.6	20	20.8 ± 25.5	24.0 ± 23.5
Micturition volume (mL)	7	234.0 ± 123.7	232.3 ± 148.0	20	178.3 ± 177.9	182.8 ± 192.6
Residual volume (mL)	7	71.1 ± 68.9	71.3 ± 66.0	20	191.2 ± 219.3	191.3 ± 204.1

* $p > 0.05$ for all variables in the comparison between hyper- and hypo-osmolar solutions and the sequence in which they were instilled.

the triggering volume of the first involuntary vesical contraction, we made an individual comparison for each patient. In 54% of the cases there was a reduction of the volume in which the involuntary bladder contraction occurred (the reduction varied from 3 to 40%) when compared hypo- and hyperosmolar solutions. Thirty eight percent of the patients presented

an increase in volume for the involuntary bladder contractions (increase from 7 to 74%) and in 8% of the cases there was no variation in volume (Table-4).

Considering the presence or absence of neuropathy, the results obtained were similar regarding the manifestation of involuntary bladder contractions as well as in the volume in which they were triggered

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and in the maximum detrusor pressure reached, independently from the fact that the solution is hyper- or hypo-osmolar, of the presence of neuropathy or not and of the sequence of instilling of solutions. Due to the small number of patients without neuropathy and with involuntary bladder contractions (n = 3), these

data were not considered in the analysis of this study. The use of the hyper- and hypo-osmolar solutions did not promote any significant change in vesical complacency, in the detrusor pressure at the end of the filling and in the functional bladder capacity in patients with or without neurological diseases (Table-5).

Table 4 – Values of urodynamic variables when vesical filling is accomplished with hyper- and hypo-osmolar solutions in patients with and without vesical hyperactivity (mean ± standard deviation).

	Without Hyperactivity			With Hyperactivity		
	N	Hyperosmolar	Hypo-osmolar	N	Hyperosmolar	Hypo-osmolar
Vesical filling phase						
Initial micturition sensation						
Volume (mL)	17	167.5 ± 145.7	159.2 ± 129.6	7	134.9 ± 74.7	157.3 ± 101.8
Pressure (cm H2O)		4.2 ± 4.4	3.1 ± 3.3		5.3 ± 4.3	8.9 ± 6.4
Habitual micturition desire						
Volume (mL)	17	307.6 ± 241.8	303.5 ± 239.1	7	185.1 ± 87.4	185.9 ± 104.8
Pressure (cm H2O)		8.8 ± 9.8	6.8 ± 5.3		22.7 ± 16.1	22.7 ± 11.7
Maximum bladder capacity						
Volume (mL)	18	414.1 ± 275.6	406.6 ± 247.6	13	202.5 ± 104.4	186.6 ± 113.4
Pressure (cm H2O)		14.6 ± 16.3	11.9 ± 12.2		7.9 ± 8.4	9.5 ± 9.0
Complacency (mL/cm H2O)	14	99.44 ± 130.23	108.5 ± 154.9	13	87.8 ± 119.9	50.0 ± 58.8
Involuntary bladder contraction						
Volume (mL)	-	-	-	13	163.9 ± 117.7	151.9 ± 112.9
Pressure (cm H2O)					70.5 ± 40.5	69.8 ± 46.8
Vesical voiding phase						
Maximum flow (mL/s)	17	9.9 ± 7.1	11.0 ± 8.0	8	11.5 ± 12.9	10.3 ± 12.7
Mean flow (mL/s)	17	5.2 ± 3.9	6.0 ± 4.5	8	5.9 ± 7.3	6.6 ± 7.9
Detrusor pressure at the maximum flux (cm H2O)	17	24.0 ± 25.9	24.4 ± 24.3	8	13.8 ± 14.7	27.5 ± 26.3
Micturition volume (mL)	17	233.7 ± 184.8	244.6 ± 203.3	8	97.5 ± 91.6	96.3 ± 97.7
Residual volume (mL)	17	192.7 ± 228.1	176.5 ± 213.2	8	120.6 ± 133.1	147.8 ± 142.0

p > 0.05 for all variables in the comparison between hyper- and hypo-osmolar solutions and the sequence in which they were instilled.

Table 5 – Values of urodynamic variables when vesical filling is accomplished with hyper- and hypo-osmolar solutions in patients with and without neuropathy (mean ± standard deviation).

	Without Neuropathy			With Neuropathy		
	N	Hyperosmolar	Hypo-osmolar	N	Hyperosmolar	Hypo-osmolar
Vesical filling phase						
Maximum bladder capacity						
Volume (mL)	19	266.9 ± 173.4	260.7 ± 128.5	14	362.0 ± 269.1	346.7 ± 268.4
Pressure (cm H ₂ O)		8.6 ± 11.9	8.4 ± 8.2		13.6 ± 14.4	12.2 ± 12.1
Complacency (mL/cm H ₂ O)	14	99.4 ± 130.2	72.6 ± 84.4	19	78.9 ± 101.3	89.5 ± 145.9
Involuntary bladder contraction						
Volume (mL)	3	127.7 ± 149.2	122.3 ± 154.0	10	174.8 ± 113.7	160.8 ± 106.6
Pressure (cm H ₂ O)		55.7 ± 36.0	46.0 ± 29.0		75.0 ± 42.5	77.0 ± 49.8

p > 0.05 for all variables in the comparison between hyper- and hypo-osmolar solutions and the sequence in which they were instilled.

COMMENTS

The concept of impermeability of the urothelium, being attributed to it the simple role of hemato-urinary barrier, has been reassessed the last few years (6,11,12). Some studies about the urothelium physiology have demonstrated the existence of an ion transport through its apical cells, which remain in direct contact with the urine (13). On the other hand, it is not yet well understood the mechanism involved in the conversion of this transcellular ion transport into nerve impulses (14). It was recently demonstrated that there are changes in various physicochemical characteristics of the urine along its trajectory from the kidney until the bladder (5). One of the most notorious is the increase in the vesical urinary osmolality when compared to the urine obtained directly from the renal pelvis. It is possible that this osmolar variation have implications in the process that involves either vesical sensitivity or the triggering of detrusor contraction. It was experimentally demonstrated in rats that the instilling of hyperosmolar solutions with acid pH lead to a reduction of the bladder capacity. The opposite occurred with the administration of alkaline and hypo-osmolar solutions (15). In this line of research the existence of a parallelism between the

oscillations of the urinary pH in the different phases of the menstrual cycle in normal women and the standard micturition behavior presented by them was evidenced. The lesser the urinary pH the more precocious and with lesser intravesical volumes the micturition desire was manifested (3). From the report of an inverse relation between urinary osmolality and cystometric capacity, it was proposed that the degree of hydration and the hydro-electrolytic balance are factors that possibly interfere in the settings of micturition urgency (16).

By developing the present study we have tried to objectively demonstrate through the performance of an urodynamic exam, the existence of a direct action of the osmolar urine composition in the vesical filling sensation and in the contractile mechanism of the urinary bladder. Observing the answer of one patient to the hypo- and hyperosmolar solutions and with the same instilling speed, we have minimized the interference of individual characteristics in the comparison of the results obtained. Another very important aspect in this work's method was the alternate instilling of solutions in each patient, removing thus the possibility of an error arising from their administration always in a similar sequence. Therefore, the urodynamic response to the hyperosmolar solution can be differentiated from the one obtained with the

hypo-osmolar solution, independently from the sequence in which they were instilled.

However, the differences obtained in this study when compared to the results of instilling hyper- and hypo-osmolar solutions during vesical filling did not reach statistic significance.

As to the detrusor motricity, it was experimentally demonstrated in rats, the largest incidence of bladder contractions after instilling a sodium chloride hypertonic solution, when compared to the isotonic solution of the same salt (6). In this sense it was already demonstrated that extracellular hyperosmolarity directly depolarize smooth muscular cells generating an increase in the detrusor activity whereas hypo-osmolarity promotes opposite responses (18). In our study, when we compared urodynamic manifestations in patients with detrusor hyperactivity, we have verified a lack of difference in urodynamic parameters utilizing both hyper- and hypo-osmolar solutions. The same lack of statistical difference in motor vesical behavior was observed in the micturition phase, compared to the results of the experimental studies described above.

Aiming at establishing if the presence of neuropathy could act as an interfering factor in detrusor hyperactivity development, as well as in the other urodynamic variables to both extreme osmolarity solutions, we have compared the results between patients bearing a neurological disease and those who did not have such commitment. There was no significant difference between both groups when exposed to different solutions, independently from the sequence in which each one was instilled.

We did not obtain different urodynamic responses when we compared both solutions with osmolarity extremes for all analyzed variables in the present study. Such fact made us precociously interrupt the study without the inclusion of new patients when the level of significance for statistical analysis was reached. We know, from what was exposed, that the variety of clinical situations of the patients involved in this study could have acted as a limiting factor in the interpretation of the results. Thus, little differences in the response during the urodynamic exam may have not reached statistical significance. On the other hand, the clinical and even the

urodynamic value in those cases are questionable.

It is also possible that the permanence contact time of each solution with the vesical urothelium, i.e., the necessary time to reach vesical plenitude, will have been insufficient for the apical cells to be adapted to the environment they were exposed to and thus, the receptors responsible for the absorption of sodium. Furthermore it is correct to suppose that hyperosmolar solutions derive from oliguria and thus, with longer contact with the urothelium, in normal physiological conditions. Ferguson emphasized in his revision on the urothelial function that the mean time to have a change in the distribution of amiloride-sensitive sodium concentration receptors is of approximately 15 minutes (14). Evidences published in the last years on a more effective action of urothelium on vesical sensitive behavior; the alteration in urinary osmolarity along the excretory system, are strong indications that a more profound research is necessary in this field of urology.

CONCLUSIONS

Vesical fillings with solutions that simulate extreme urinary osmolarities, performed with similar speed and without previous identification do not alter sensitive or motor urodynamic behavior in patients of the present study. To our knowledge, it is the first double-blind study in the literature where 2 solutions that simulate extreme urinary osmolarities (hyper- and hypo-osmolarities), were tested during an urodynamic study.

CONFLICT OF INTEREST

None declared.

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