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ORIGINAL ARTICLE

Usefulness of ice water test to unmask detrusor overactivity



Utilité du test à l'eau glacée pour démasquer un détroleur hyperactif

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KEYWORDS

Ice water test;
Bladder cooling reflex;
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Summary

Purpose. – Ice Water Test (IWT) is not frequently used today. IWT triggers a non-inhibited involuntary detrusor contraction (NIDC) when the bladder is being filled with cold saline solution. NIDC is unmasked via a segmental reflex loop different from the physiological micturition reflex. Our purpose was to search for usefulness of IWT to expose detrusor overactivity (DO).

Methods. – One hundred and seventy-nine IWT performed in patients with overactive bladder syndrome (OAB) and conventional cystometry (CC) non-contributive to diagnosis were retrospectively analyzed. An increase of detrusor pressure of 15 cm H₂O allowed defining positive IWT (with leakage) or intermediate (without leakage).

Results. – The population comprised of 131 women (58.2 ± 17.3 years) and 48 men (56.1 ± 15.3 years). Main complaints were mixed or urge incontinence (76/179). Hundred and twenty-four patients had a history of neurological disease. From CC, detrusor behavior was found uncategorized for 106, normal for 53 patients and underactive for 20. These results did not contribute to diagnose a DO. IWT was positive for 22 patients and intermediate for 20. DO was unmasked by IWT for 42 patients (23.4%) of whom 34 had neurological disease. The positive predictive value was 80.9%, the negative predictive value was 34.3%.

Conclusion. – In patients with OAB syndrome, IWT is contributory to unmask DO when CC is not contributive. Our study underlines the interest to perform IWT when urodynamic diagnosis is unclear.

Level of evidence. – 4.

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MOTS CLÉS

Test à l'eau glacée ;
Vessie neurologique ;
Urodynamique ;
Neuro-urologie

Résumé

But. — Le test à l'eau glacée (TEG) est peu utilisé en pratique courante. Il déclenche une contraction non inhibée du détrusor (CNID) quand la vessie est remplie par du sérum physiologique froid. Cette CNID est déclenchée via une boucle réflexe segmentaire différente du réflexe mictionnel physiologique. Le but de l'étude était de rechercher l'utilité du TEG pour démasquer une hyperactivité du détrusor (HD).

Méthodes. — Rétrospectivement, 179 TEG réalisés chez des patients se plaignant d'un syndrome d'hyperactivité vésicale sans observation de CNID à la cystomanométrie ont été analysés. Une augmentation de la pression détrusorienne de 15 cm d'eau permettait de définir un TEG positif (avec fuites) ou intermédiaire (sans fuite).

Résultats. — La population comprenait 131 femmes ($58,2 \pm 17,3$ ans) et 48 hommes ($56,1 \pm 15,3$ ans). Le motif principal de consultation était une incontinence mixte ou par urgenturie (76/179). Cent vingt-quatre patients avaient une pathologie neurologique. À la cystomanométrie, l'activité du détrusor était indéterminée pour 106, normale pour 53 et hypoactive pour 20. Ces résultats ne permettaient pas de diagnostiquer une hyperactivité détrusorienne. Le TEG était positif chez 22 patients et intermédiaire chez 20. Une hyperactivité du détrusor a été démasquée chez 42 patients (soit 23,4%) dont 34 avaient des antécédents neurologiques. La valeur prédictive positive était de 80,9%, la valeur prédictive négative de 34,3%.

Conclusion. — Chez des patients ayant un syndrome d'hyperactivité vésicale, le TEG contribue à démasquer une hyperactivité détrusorienne lorsque la cystomanométrie n'a pas permis de conclure. Notre étude souligne l'intérêt de pratiquer le TEG quand l'urodynamique « standard » n'a pas permis d'affirmer le diagnostic.

Niveau de preuve. — 4.

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Introduction

IWT was first described in 1957 by Bors and Blinn [1]. It was useful to discriminate between spinal cord injury (SCI), upper (UMN) and lower motoneuron (LMN) lesions associated with neurogenic bladder. Animal and clinical studies have given more explanation on characteristics of IWT [2–4]. It uses a lower motoneuron segmental reflex involving cold receptors and C fiber afferents [3,5]. IWT is positive in subjects less than 5 years old, negative after because central inhibition exists [3]. Recall that physiological micturition reflex uses a different pathway implying mechanoreceptors, A δ fibers and pontine reflex. Our purpose was to analyze IWT of patients with neurological condition in order to unmask detrusor overactivity (DO); a control population was patients without neurological condition. These patients complained of overactive bladder (OAB) syndrome without DO during Conventional Cystometry (CC). Could IWT be a help to diagnose DO?

Materials and methods

Retrospectively, 179 IWT of patients whose complaint was suggestive of OAB syndrome were analyzed. Detrusor function during CC was identified as normal, uncategorized or underactive. Normal detrusor function is the presence of

a clear detrusor contraction during voiding. Uncategorized detrusor function is the absence of detrusor contraction or an impossible voiding in seated position. According to the definition of the International Continence Society, detrusor underactivity is a detrusor contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span. After CC, patients underwent IWT to search for hidden DO.

In literature, IWT is always negative in healthy people, stress incontinence or bladder painful syndrome. IWT can be positive with neurological disease (UMN), obstruction, infection. Historically, IWT was described negative in neurological patients with 2nd motoneuron dysfunction (i.e. LMN).

All patients had an evaluation including a detailed medical history, review of medications, bladder diary for at least 48 h including voiding times and voided volumes both day and night, physical examination and dipstick urinalysis. If neurological disease is known, we try to precise it clinically or radiologically. If patient do not know, we practice easily a clinical examination, cerebral and medullar RMN.

CC was performed with the patient in seated position with a 7-F triple-lumen urethral catheter perfused with saline at room temperature using a filling rate of 50 ml/min. Pressure transducers were zeroed to atmospheric pressure at the upper edge of the symphysis pubis. Rectal pressure was recorded using a punctured intrarectal balloon catheter

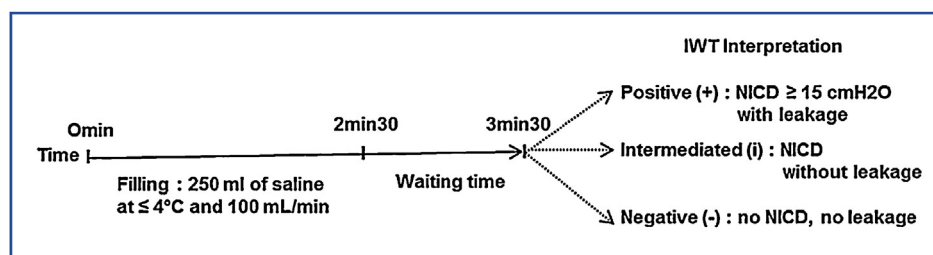


Figure 1. Schema of IWT protocol; performed bladder empty after CC.

filled with 2 mL of saline according to the report of Good Urodynamic Practice guidelines [6].

IWT was performed after CC. Starting from bladder empty, 250 mL of saline at $\leq 4^{\circ}\text{C}$ (available in a fridge) were instilled at 100 mL/min. Filling was followed by a waiting time of 1 min. Pressures (vesical, rectal) and flow rate were recorded during filling and waiting time. Patients were asked not to void. IWT was defined as positive if a non-inhibited detrusor contraction (NIDC) ≥ 15 cm of water with leakage occurring within 3.5 min (filling plus waiting time); intermediate in case of NIDC without leakage and negative in case of absence of any detrusor contraction (Fig. 1).

Statistical analysis

Statistical analyses were performed using SAS, version 5.0 (SAS Institute, Inc., Cary, NC).

The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and confidence interval (CI 95%) were calculated.

Sensitivity was defined as the ratio between true positives (neurological patients [NP] with positive IWT) and the sum true positives plus false negatives (equal NP). Specificity was defined as the ratio between true negatives (non neurological patients [NNP] with negative IWT) and the sum true negatives plus false positives (equal NNP). PPV was defined as the ratio between true positives and the sum true plus false positives (positive IWT). NPV was defined as the ratio between true negatives and the sum true plus false negatives. With a high PPV, a positive result asserts the diagnosis of DO. With a high NPV, negative result allows to exclude the diagnosis of DO.

Results

The population comprised of 179 patients, 131 women (mean age: 58.2 ± 17.3 years) and 48 men (mean age: 56.1 ± 15.3 years). One hundred and twenty-four patients had neurological disease (83 women, 41 men). Main complaints were mixed or urge incontinence (76/179). Characteristics of the population are described in Table 1.

From CC (Fig. 2), detrusor behavior was found underactive in 20, normal in 53 patients and uncategorized in 106. IWT's results are presented depending on neurological status. In the whole population, IWT was positive or intermediated in 42 patients (23.4%).

Table 1 Symptoms and diagnoses in the studied population.

	Ratio men/women	131/48
Symptoms	Urgency	11
	Urge incontinence	28
	Mixed incontinence	48
	Stress urinary incontinence	18
	Frequency	25
	Retention	72
	NP	
UMN		80
	Encephalic	34
	MS	21
	SCI	25
	LMN	44
	Cauda equina syndrome, lumbar spinal stenosis, neuropathy, pelvic lesion, myasthenia, myopathy. . .	
NNP	POP, chronic retention, polypathology. . .	55

LMN: lower motoneuron; MS: multiple sclerosis; NNP: non neurological patient; NP: neurological patient; POP: pelvic organ prolapse; SCI: spinal cord injury; UMN: upper motoneuron.

Among the 124 neurological patients (NP), detrusor was found underactive in 15, normal in 31 and uncategorized in 78. IWT was positive or intermediate in 6 patients with underactive detrusor, 8 patients with normal detrusor activity and 20 patients with uncategorized detrusor activity. So, IWT was positive or intermediated in 34/124 NP (27.4%). In other words, if IWT was not performed in NP, DO would not be diagnose in 34/124 patients (27.4%).

Among the 55 non-neurological patients (NNP), IWT was found less frequently positive or intermediated than for NP; only 8 IWT (14.5%) were positive or intermediate when CC was not helpful to conclude of DO.

Clinical status of patients versus IWT result is described in Table 2. IWT was positive or intermediated in 34 NP versus 8 NNP.

Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and the confidence interval (CI) were given in Table 3. The most interesting result was PPV equal 80.9% for NP. These findings will be detailed in the discussion.

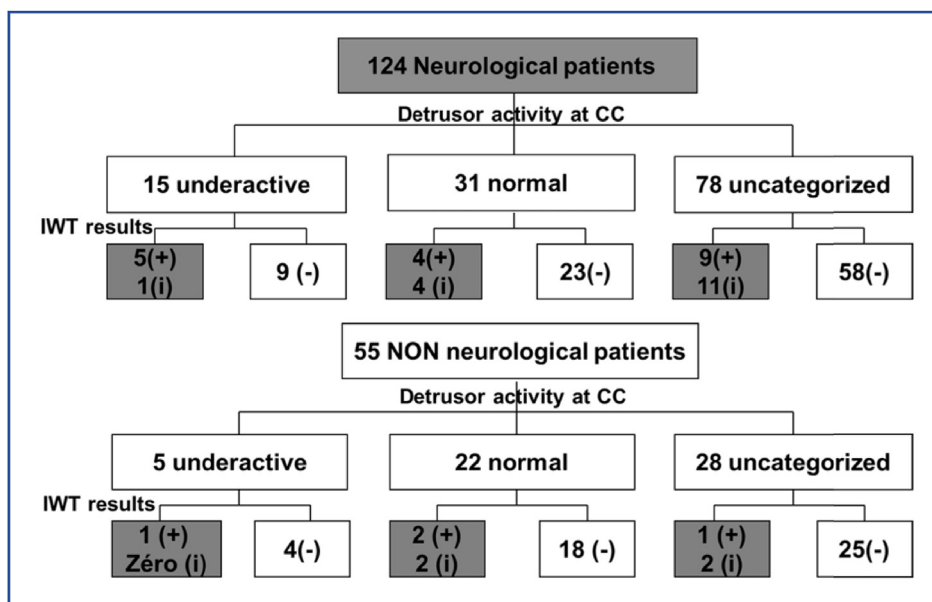


Figure 2. Results of conventional cystometry (CC) and IWT depending on neurological status. (+): positive; (i): intermediate; (-): negative.

Table 2 IWT result versus neurological diagnosis.

IWT result		22 (+)	20 (i)	137 (-)
NP	UMN	17	12	51
	Encephalic	9	3	22
	SCI	5	4	16
	MS	3	5	13
	LMN	1	4	39
NNP		4	4	47

LMN: lower motoneuron; MS: multiple sclerosis; NNP: non neurological patient; NP: neurological patient; SCI: spinal cord injury; UMN: upper motoneuron.

Discussion

IWT was first described in 1957 by Bors and Blinn [1]. They studied cold receptors and used IWT as a provocative test to discriminate upper from lower motor neuron lesions. They

concluded that positive IWT was a marker of an upper motor neuron lesion (UMN).

IWT induces a lower motoneuron segmental reflex involving C-fiber afferents, which are associated with cold receptors TRPM8 in the bladder wall [4,5,7–9]. This reflex is present in subjects less than 5 years old; after this age, there is a central inhibition. It can appear again when there is inflammation or infection of the bladder, urethral obstruction, neurological lesion [3,10–14].

To have a positive IWT, the following conditions have been chosen: temperature of infused fluid <4°C, filling rate of 100 mL/min, a detrusor contraction higher than 15 cm H₂O and fluid expulsion during filling plus waiting time. These conditions have to be discussed according to the results in literature [2,3,10,15].

A first question arises because inside of bladder is near 37°C and because fluid temperature warm up very quickly. Initially, ice-water (0 to 2°C) was used [1]. Geirsson et al. found that human bladder cooling reflex (indicated by positive IWT) is observed if expelled fluid has temperature below 18°C and filling rate higher than 100 mL/min [2]. The same conclusion has been demonstrated by Mukerji et al. [8].

Table 3 Results of IWT in the studied population.

Population			
IWT	NP	NNP	Total
Positive	34	8	42 (PPV = 80.9%)
Negative	90	47	137 (NPV = 34.3%)
Total	124	55	179

Positive predictive value (PPV), negative predictive value (NPV), sensibility (Se), specificity (Spe)

PPV [95% CI]	NPV [95% CI]	Se [95% CI]	Spe [95% CI]
80.9% [69.1–92.7]	34.3% [26.4–42.2]	27.4% [19.6–35.2]	85.4% [76.1–94.7]

A second question is the effect of filling rate. In 1957, IWT was described with a filling of 60 mL in 30 s [1]. In addition to temperature, many researchers have modified the infusion speed and the volume of fluid [3]. If the changes in conditions of the test induce difficulties to compare the results obtained by the investigators, it appears that the best results are obtained with a filling rate higher than 100 mL/min and a filling volume equal to half cystometric capacity, 250 mL in our study. In conclusion, colder is the water and higher is the filling rate, better and franker will be the response of IWT.

In 1999, Geirsson et al. wrote that it is important to compare detrusor pressure during micturition in CC and in IWT. The cut-off value for the difference between maximum detrusor pressure during IWT and CC is 30 cm H₂O [15]. Other authors proposed a cut-off value of 20 cm H₂O for positive results [3]. Hellström et al. found that the test was negative when detrusor contraction was lower than 15 cm H₂O [16]. Today, it seems reasonable to interpret intermediate IWT when there is some detrusor contraction even if there is no fluid expulsion. This interpretation is like a detrusor-sphincter dyssynergia with an overactive detrusor.

IWT is easy to perform, has poor side effects, is cheap but rarely used. It needs only to keep water at the desired temperature near the urodynamic room, this in order to avoid the patient to be anxious and preserve the response of the IWT (possible central inhibition?).

In SCI population, caregivers have to be careful of autonomic hyperreflexia when they do it. In bladder pain syndrome, IWT is very painful (but still negative), TRPM8 is overexpressed in detrusor wall and nevertheless, IWT is negative in that case. . . Hypothesis is when IWT is positive, central inhibition are suspended [17].

Characteristics of our population do not differ of those of the population presenting with OAB syndrome. Urgency is more frequent in women. Main complaints are mixed or urge incontinence; these symptoms are usual in OAB syndrome. The main part of our population comprises NP for whom CC is not sufficient to confirm a neurological bladder. IWT is useful to go ahead in the diagnosis.

In our population, IWT is positive or intermediate for 42 patients (Table 2), most of them have neurological lesion: 12 encephalic, 9 SCI, 8 MS and 5 LMN. Among these patients, 8 have not a neurological condition: 2 geriatric, 1 urethral obstruction, 2 OAB syndrome, 1 Pelvic Organ Prolaps (POP), 1 multiple pelvic surgery and 1 bladder pain syndrome. IWT can be positive in these situations and proved in recent study [3,11]. An unexpected result is to find a positive IWT for a patient who presents a bladder pain syndrome. In this condition, IWT is commonly painful but does not induce detrusor contraction.

Initially, IWT was described as specific of UMN lesion. Few studies later show that a lot of pathologies can reemerge this segmental reflex (under bladder obstruction, idiopathic DO. . .).

Peterson et al., in 1997, were using IWT to discriminate in NP DO versus bladder instability. For IWT, the overall sensitivity was 65% and specificity 85%. The positive predictive value was 93% and negative IWT only predicted a non-neurogenic disorder in 45% of patients [18].

In the present study (Table 3), sensitivity and specificity are not discussed because they are only useful for overall

population. PPV is 80.9% but NPV 34.3%. So, a good prediction of DO in NP with OAB and uncategorized CC is obtained using IWT. Conversely, due to the low value of NPV, a negative IWT does not allow eliminating DO. Some prospective studies should be done.

Usually, urodynamic testing does not include IWT. However, it is important not to ignore its existence. A question is: does performing IWT change our management? IWT can contribute to the thought process leading to a more accurate diagnosis. Thus, it can help to make the good choice for management, for propose treatment and for follow-up of each patient (screening possible complications) [3,19,20].

Recall that, in 2010, an interesting proposal of Al Hayek and Abrams [3] described 9 applications of IWT:

- differentiating upper from lower motoneuron lesions;
- as an early prognostic tool indicating the integrity of spinal segments in patients recovering from spinal injury;
- as a provocative test in urodynamics cases showing DO when standard urodynamics failed to do so;
- making a specific diagnosis in patients with bladder outlet obstruction and possibly predicting the outcome of transurethral prostate resection;
- categorizing different overactive bladder types;
- detecting masked neurological conditions;
- differentiating between external sphincter spasm and bladder neck obstruction in patients with UMN lesions;
- therapeutic role in treating hyporeflexia or areflexia caused by psychogenic inhibition;
- as a marker for recruiting and assessing efficacy in painful bladder syndrome clinical trials.

First limitation of our study is to be retrospective and further prospective studies must be conducted. Second limitation is our inclusion bias, VPP and VPN values are calculated in a specific population. Generalization of our results is difficult and could be devoted to a clinician studying similar population.

Conclusion

IWT exists since more than 55 years and its contribution to diagnose neurological bladder increases. IWT allows unmasking DO in patients with history of neurological disease whose CC gave no reliable conclusion on the detrusor behavior. IWT is simple, not money-consuming and easy to perform. Thus, IWT appears as a valuable complement of urodynamics and must be performed when the CC of a patient complaining of urgency leads to an ambiguous conclusion. A prospective study is necessary to confirm this finding.

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Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.purol.2015.05.007](https://doi.org/10.1016/j.purol.2015.05.007).

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