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Use of the ice water test as an early predictor of recovery of erectile function in patients with spinal cord injury

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Abstract

Study design Retrospective, cross-sectional.

Objectives To determine the capacity of the ice water test (IWT) to predict erectile function during the early phase of spinal cord injury (SCI).

Setting France.

Methods This was a retrospective, cross-sectional study. Data from patients with SCI were included if they presented with neurogenic shock causing erectile dysfunction AND detrusor underactivity, and had undergone the following evaluations during the first 6 months post SCI (E1), and again at least 2 years later (E2): a complete neurological examination, urodynamic evaluation with the IWT, and evaluation by the Erection Hardness Score (EHS, from 0 to 4). Patients with cauda equina syndromes were excluded.

Results Data from 62 patients with SCI were included, 37 with a positive IWT and 25 with a negative IWT. E1 was performed at 3.2 months \pm 1.9, and E2 at 2.0 years \pm 2.9 post SCI. At E2, 95% of patients with an initial positive IWT had reliable erections (EHS 3 or 4), compared with 0% of patients with a negative IWT. Neurogenic detrusor overactivity was found in 89% of patients with a positive IWT compared with 8% with a negative IWT. The IWT had a good sensitivity and negative predictive value: 100% for erectile function, and respectively 94 and 92% for bladder function.

Conclusion The IWT is a reliable and predictive test of erectile potential in patients with sacral and suprasacral SCI.

Introduction

The prediction of sexual function following spinal cord injury (SCI) requires a comprehensive neurological clinical examination, including assessment of both somatic and autonomic function of the segments concerned. To evaluate the somatic pathway, the bulbocavernosus reflex or the anal wink can be used to determine whether the sacral lesion is caused by upper or lower motor neuron (UMN/LMN) injury

and helps predict the type of sphincter dysfunction, especially in patients with complete SCI [1–4].

In the immediate aftermath of a traumatic SCI, a state of spinal shock is usual. This corresponds to a loss of excitability of the spinal cord, with a decrease in autonomic activity as well as somatic activity [5]. This state is transient and, as a rule, somatic reflexes return in a cephalad direction with the anal and bulbocavernosus and plantar reflexes returning first [5]. However, the loss of autonomic reflexes can last longer, for weeks or even months after the SCI [6, 7]. This particular state, sometimes referred to as neurogenic shock, explains why erectile dysfunction and detrusor underactivity or areflexia may persist.

The ice water test (IWT) has been used to evaluate the contractile potential of the bladder in both animals and human subjects for many years [8]. This test was first used in patients with SCI in 1957 by Bors to differentiate between suprasacral and sacral lesions [9]. They carried out the IWT with urodynamic measurements to determine the contractile potential of the detrusor muscle. In individuals with SCI, the micturition reflex is a sacral parasympathetic

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reflex mediated by C-fibres and is not under supraspinal control. Bladder function, the rectal ampulla and the erection reflex are controlled by the pelvic nerve, which is parasympathetic, and arises from the S2–S3–S4 spinal segments. The IWT is useful to determine the integrity of the whole parasympathetic sacral system, including erectile capacity. Early determination of reflex erectile potential using a predictive test such as the IWT would help to optimise management of sexual function in patients with SCI.

The aim of this study was, therefore, to determine the capacity of the IWT to predict erectile function in the early phase of SCI, in patients presenting with severe or lasting neurogenic shock characterised by erectile dysfunction and detrusor underactivity or areflexia.

Materials and methods

This was a retrospective, cross-sectional study carried out using the files of patients admitted to the Bouffard-Vercelli Neurological Rehabilitation Centre, Cerbère (France). According to current French legislation, IRB approval is not required for retrospective studies.

Inclusion criteria

Adult men above the age of 18 years were only included if they met all the following criteria:

- SCI less than 6 months
- Cervical, thoracic or thoraco-lumbar bony injury of traumatic origin
- Neurogenic shock with erectile dysfunction (penis not hard enough for penetration) AND detrusor underactivity or areflexia (urodynamic testing)
- First assessment within 6 months of the injury (E1)
- Second assessment at least 2 years later (E2)

Patients were not included in case of a cauda equina syndrome relating to a lumbar bony injury (below L2 vertebra), if the files did not contain complete data or if they had any associated pathology or treatments that could alter bladder and sphincter or sexual functions.

Evaluations

Clinical exam:

- A neurological examination to determine the neurological level of the lesion using the International Standards for Neurological Classification of SCI (ISNCSCI) and the ASIA Impairment Scale: complete motor lesions are

classified as levels A or B and incomplete motor lesions as C or D [10].

- A clinical examination of the perineum, including the bulbocavernosus reflex, the nociceptive anal reflex, anal tone, S2–S3–S4 sensation and activity of the anal sphincter. The results determined if the lesion level was UMN (sacral reflexes present or exaggerated) or LMN (sacral reflexes abolished).

- A thoraco-lumbar bony injury was defined as a sacral lesion (conus medullaris syndrome) and a cervical or thoracic bony injury was defined as a suprasacral lesion (tetraplegia or paraplegia).

Urodynamic testing:

- A filling cystometry performed according to the norms determined by the International Continence Society [11]. This assessment was carried out using a Geyre Electronic 2500C (MMS) device with a filling rate of 50 ml/min. The amplitude of detrusor contractions (DCs) was analysed whether the detrusor was over- or underactive. It was calculated by subtracting abdominal pressure from vesical pressure [11].

- An IWT using sterile water at 4° at a perfusion rate of 100 ml/min. This rapid filling method with iced water was used if the standard urodynamic examination failed to elicit a DC. The amplitude of the DC and the volume of cold water required to trigger it were recorded. The test was considered positive if the amplitude of the DC was ≥ 30 cm H₂O at a volume of <250 ml. These values were based on other studies in the literature and confirm the DC [12]. A neuro-urologist who had not carried out the initial assessments re-interpreted all the urodynamic testings according to Geirsson's criteria [12]. The IWT was only carried out at E2 in case there was no DC during the second urodynamic testing.

Assessment of erectile function:

- Erectile function was rated on the Erection Hardness Score (EHS) from 0 'Penis does not enlarge' to 4 'Penis is completely hard and fully rigid' [13]. Rigidity was considered as satisfactory if the EHS was ≥ 3 'Penis is hard enough for penetration, but not completely hard'.

Statistical analysis

The sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated for the IWT to determine its predictive value. Se measures the proportion of actual positives that are correctly identified. Sp measures the proportion of actual negatives

that are correctly identified. Sp was calculated by dividing the number of true positives by the sum of the true positives and false negatives.

PPV represents the proportion of positive results that are true positives. It was calculated by dividing the number of true positives by the sum of the true positives and false positives.

NPV represents the proportion of negative results that are true negatives. It was calculated by dividing the number of true negatives by the sum of the true negatives and false negatives.

The frequency of patients with a positive IWT and an EHS < 3 was compared between E1 and E2 with a Fisher test. $p < 0.05$ was considered significant in all cases. Values in brackets show ranges. Statistical analysis was performed with software from the biostatTGV site.

Results

Sixty-two patients met the inclusion criteria (Table 1). The details of the clinical and autonomic examinations are provided in Tables 2 and 3.

E1 was performed between 0.4 and 6 months post SCI (mean 3.2 months \pm 1.9). The EHS ranged from 0 to 2 (mean 1.4 \pm 0.6). The IWT was negative for 25 patients and positive for 37 patients, with DC ranging from 30 to 140 cm H₂O. All but one patient who had a positive IWT test had an UMN lesion, whereas all patients in the negative IWT group had an LMN lesion.

E2 was performed 2.0 years \pm 2.9 post SCI (0.2–15.8). The neurological status (ISNCSCI and AIS) and perineal status (UMN or LMN) had not changed.

Erectile function at E2 (Table 4) was significantly improved in the positive IWT group, with a mean score of

3.8/4. For 35 out of the 37 patients (95%) the EHS was \geq 3. By contrast, erectile function was not improved in the negative IWT group as none of the 25 patients had an EHS score above 2 (mean 1.0).

Se and NPV of IWT for erectile function were 100%. Sp and PPV were respectively 93 and 95%.

Bladder function at E2 (Table 5), 33 out of 37 patients (89%) in the positive IWT group showed neurogenic detrusor overactivity with spontaneous DC > 30 cm H₂O during filling cystometry, compared with only 2 out of 25 patients in the negative IWT group.

Se and NPV of IWT for bladder function were respectively 94 and 92%. Sp and PPV were respectively 85 and 89%.

When neurogenic detrusor overactivity (NDO) was found at E2, 31 patients had concomitant reliable erections (EHS \geq 3) while 4 did not. With a detrusor underactivity at E2, only 4 of the 27 patients showed concomitant good erections (Table 6).

In case of a positive IWT, 97% of patients with a suprasacral lesion recovered an EHS \geq 3 (32/33) vs. 75% (3/4) of those with a sacral lesion, and 89% (33/37) vs. 100% (4/4) of patients had NDO, respectively. When the IWT test was negative, none of the patients with sacral (0/21) or suprasacral (0/4) lesions recovered satisfactory erections (all EHS \leq 2), while neurogenic detrusor overactivity was found in one patient with a sacral lesion (1/21, 5%) and in another with a suprasacral lesion (1/4, 25%).

The outcome was significantly different according to the type of lesion, with 94% of patients with a UMN lesion (34/36) improving their erectile function with an EHS \geq 3 compared with only 4% of those with an LMN lesion (1/25) ($p = 0.012 \times 10^{-11}$). Similarly, 89% of patients with a UMN lesion (34/36) had NDO compared with only 8% of those with an LMN lesion (2/25) ($p = 0.021 \times 10^{-10}$).

Table 1 Patient characteristics.

	IWT E1	Positive	Negative
	Number	37	25
	Mean age (years)	39.5 \pm 17.1 (18.0–72.2)	32.7 \pm 15.1 (17.2–69.2)
Level of the lesion	Cervical (<i>n</i>)	20	0
	Thoracic (<i>n</i>)	13	4
	Lumbar (conus) (<i>n</i>)	4	21
Mean time since SCI		3.2 \pm 1.9 months (0.4–6.0)	2.0 \pm 2.9 years (0.2–15.8)
ASIA impairment scale	A – B (complete) (<i>n</i>)	33	22
	C – D (incomplete) (<i>n</i>)	4	3
Motor neuron lesion	UMN (<i>n</i>)	36	0
	LMN (<i>n</i>)	1	25

For age and time since SCI, the mean \pm standard deviation (range) are presented.

IWT ice water test, E1 first evaluation, SCI spinal cord injury, AIS ASIA Incapacity Scale, UMN upper motor neuron, LMN lower motor neuron, *n* number.

Table 2 Autonomic and neuro-perineal examination of the 37 patients with spastic SCI.

	Anal tone	Voluntary anal contraction	Sacral somatic sensation	Sacral reflex ^a	Somatic sensation T10-L1	T12-L1 reflexes ^b
Absent (<i>n</i>)	1	33	24	0	28	4
Reduced (<i>n</i>)	–	4	13	0	6	3
Normal (<i>n</i>)	36	0	0	37	3	31

n number.

^aBulbocavernosus/bulbo-anal reflexes.

^bScrotal and cremasteric reflexes.

Table 3 Autonomic and neuro-perineal examination of the 25 patients with flaccid SCI.

	Anal tone	Voluntary anal contraction	Sacral somatic sensation	Sacral reflex ^a	Somatic sensation T10-L1	T12-L1 reflexes ^b
Absent (<i>n</i>)	22	22	17	25	11	15
Reduced (<i>n</i>)	3	3	8	0	2	2
Normal (<i>n</i>)	0	0	0	0	12	8

n number.

^aBulbocavernosus/bulbo-anal reflexes.

^bScrotal and cremasteric reflexes.

Table 4 Results of IWT and erection function.

IWT	EHS	E1	E2
Positive (<i>n</i> = 37)	Mean scores	1.6 ± 0.5 (1–2)	3.8 ± 0.6 (1–4)
	Score of 3 or 4 (<i>n</i>)	0	35
	Score of 0–2 (<i>n</i>)	37	2
Negative (<i>n</i> = 25)	Mean scores	1.0 ± 0.7 (0–2)	1.2 ± 0.7 (0–2)
	Score of 3 or 4 (<i>n</i>)	0	0
	Score of 0–2 (<i>n</i>)	25	25

For the mean scores, the mean ± standard deviation (range) are presented.

IWT ice water test, E1 first evaluation, E2 second evaluation, EHS Erection Hardness Score, *n* number.

Table 5 Results of IWT and detrusor activity.

IWT	Neurogenic detrusor activity	E1	E2
Positive (<i>n</i> = 37)	Overactivity (<i>n</i>)	0	33
	Underactivity (<i>n</i>)	37	4
Negative (<i>n</i> = 25)	Overactivity (<i>n</i>)	0	2
	Underactivity (<i>n</i>)	25	23

IWT ice water test, *n* number, E1 first evaluation, E2 second evaluation.

Discussion

The results of this study showed that the IWT carried out in the early phase of SCI is predictive of recovery of erectile function in men with SCI. A search of the scientific

Table 6 Relationship between IWT and erectile function.

IWT	Neurogenic detrusor activity	EHS 0–2	EHS 3–4
Positive (<i>n</i> = 37)	Overactivity (<i>n</i>)	2	31
	Underactivity (<i>n</i>)	0	4
Negative (<i>n</i> = 25)	Overactivity (<i>n</i>)	2	0
	Underactivity (<i>n</i>)	23	0

IWT ice water test, EHS Erection Hardness Score, *n* number.

literature including PubMed did not reveal any other articles describing use of the IWT for this purpose.

The advantage of the IWT is that it is quick and simple to perform and repeat. Other tests, such as Rigiscans [14], are more complex to perform and moreover, Rigiscans do not predict recovery of erectile function. Qualitative and subjective evaluations of erection, such as the International Index of Erectile Function [15], also cannot predict recovery. Testing of the bulbocavernosus reflex to evaluate or predict autonomic function is limited by the fact that the clinical or electrophysiological presence of that reflex reflects below-lesion sacral somatic activity.

Since its original description by Bors, the physiopathology of the IWT has been well documented [8, 9]. Studies in anesthetised animals have shown that the perfusion of iced water into the bladder can trigger contraction of the detrusor muscle. This reflex is not based on the usual neurological circuits that involve mechanoreceptors of the bladder and A delta afferent fibres [16–18], instead iced water has been shown to stimulate thermoreceptors, which are mediated by suburothelial TRPM8 receptors [17, 19] found in both

animals and humans [20–22]. Intra-vesical C-fibres are then activated, and afferent information is transmitted via the parasympathetic pelvic nerve. This reflex is modulated by suprasacral neurological structures which inhibit it from the age of 5 years [23, 24]. In healthy adults, the IWT is negative, simply generating a pressing need to urinate, without DC [23, 24].

In the literature, the criteria on which a positive IWT are based are heterogenous: amplitude of the DC, filling speed, perfusion volume required to trigger it, the water temperature (pre and post IWT) and time before interpretation all vary [25]. We chose to use the most commonly reported values of 30 cm H₂O, at a volume above 50% of the cystometric volume, with a filling speed of 100 ml/min to define DC during the IWT. The temperature of the water used was always 4° or less, and the evaluation was carried out up to one minute post IWT since DC may occur up to that time [12].

The relationship between a positive IWT and UMN lesions has been largely demonstrated [9, 26]. The Se and/or PPV of the IWT have been reported for NDO, detrusor external sphincter dyssynergia [26, 27], the recovery of low-level SCI and for the early diagnosis of central neuropathy [28–30]. Ninety-seven percent of patients with SCI have a positive IWT [20] and the test is always negative in the case of sacral and LMN lesions [8]. The results of this study (89%) are in line with those of the literature.

In their pilot study in 1960, Bors and Comarr found that 93% patients with complete UMN lesion had reflex erections, but that intercourse (successful coitus) was possible in only 53% of them [31]. Those reflex erections were absent in patients with complete LMN lesions (0%). However, the correspondence between somatic and vegetative activity is less accurate in other syndromes like epiconus or conus medullaris, where a mixed picture of UMN (due to the cell body damage of motor neurons in the conus and/or nerve root injury), and LMN symptoms (due to nerve root injury) is present. In those syndromes, the presence of sacral reflexes (i.e., bulbo-cavernosus and anal wink) helps distinguish this syndrome from a cauda equina injury [10, 32–34]. The IWT, which shares common neurological pathways with reflex erections, is thus a useful addition to better predict the erectile potential of those men.

Conclusion

This study showed that the IWT is a simple and reliable test that evaluates the integrity of the whole sacral parasympathetic system. The results of the test predict erectile potential in patients with sacral and suprasacral SCI. Early evaluation of erectile potential allows the prognosis of

erectile function to be determined and appropriate treatments to be administered.

This study highlights the need to add more information to the ISNCSCI examination regarding sacral function. Routine performance of sacral reflexes allows classification of lesions as UMN or LMN, which should be part of the ISNCSCI. Adding the sacral component of the International Standards for the Assessment of Autonomic Function after SCI to the ISNCSCI examination is another option [3, 34–37].

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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