

Is there a relationship between chronic bladder dysfunction and somatic symptoms in other body regions? 1. Clinical observations

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Abstract. *Objective:* Investigation of patients with chronic bladder dysfunction regarding associated general symptoms and complaints in the cervico-facial, upper and lower extremity regions. *Patients and methods:* We retrospectively evaluated history, physical and special neurourological examination and urodynamic studies in 213 patients with non-neurogenic bladder dysfunction. *Results:* 22 patients out of 213 patients with chronic bladder dysfunction reported reproducible associated symptoms involving the temporo-mandibular joint, the distal forearm/hand or feet and headache. There was an obvious clinical connection regarding the severity of bladder dysfunction and associated symptoms and possible relief of both by successful treatment. *Conclusion:* Symptomatic lower urinary tract dysfunction may be accompanied by specific muscular and/or sensory disturbances in different areas of the body. These associated pathologies in patients without neurological disease can be explained by functional changes in a complex autonomic peripheral and central nervous network.

Key words: Bladder dysfunction, Central nervous system, Chronic pain, Headache

Introduction

Patients with symptomatic lower urinary tract dysfunction, not uncommonly, have associated symptoms in seemingly unrelated areas of the body. Vague symptoms distributed in the cervico-facial region, upper and lower extremities, as well as headache and emotional disturbances are reported often enough by patients that it is reasonable to query whether or not these symptoms are somehow linked to the underlying bladder dysfunction [1]. More specifically, patients with voiding dysfunction commonly report pelvic pain [2] along with discomforts in other regions – headache, impairment of taste, hearing and sight, temporo-mandibular-joint (TMJ) syndrome, altered sensorium and/or weakness in the upper/lower limb(s).

The relationship between somatic and autonomic symptoms in neurogenic voiding dysfunction, i.e. spinal cord injury, is well recognized

[3–5]. Often described, inherent complications are related directly to the bladder dysfunction (e.g. hydronephrosis, renal dysfunction, nephrolithiasis, bladder wall fibrosis) and to an aberrant reflex neuronal network (e.g. basal hypotension, hypertensive crisis with danger of stroke and palsy, excessive sweating, headache) [3, 6, 7].

Given the clear association of autonomic symptoms (dysreflexia) with bladder dysfunction in spinal cord injury based on a gross disturbance of central neuronal pathways, the potential for such linkage is poorly understood, dysfunctional states seem feasible [8]. Minor anatomical or biochemical changes at the cellular level in central or peripheral neuronal pathways may be responsible for dysfunctional symptoms in different areas of the body.

Lower urinary tract dysfunction without neurological disease are classified as simply dysfunctional or non-neurological bladder dysfunction (Hinman–Allen-Syndrome) [9].

It emerges the question if there is a clinic correlation which allows to hypothesize that somatic non-urolological and urological symptom in one individual may have the same pathophysiological roots. This would change our diagnostic and also therapeutic approach.

A systematic review of symptoms reported by patients being treated in a voiding dysfunction clinic was therefore carried out.

Patients and methods

A standardized approach in the Neuro-Urology/Pelvic Pain Clinic is used for all new patients allowing for retrospective data collection. The reviewed patient pool was highly selective, in that all had been referred to the University clinic after failure/of available community based therapies.

First a data sheet is completed by all patients. This is then reviewed by the specialized urologist for completeness or misinterpretation on the part of the patient. A medical profile is thus obtained which includes previous medical history, and a current, complete, reliable symptomatic review of all systems. A micturition diary for a period of 14 days is completed by all patients.

The clinical investigation of every patient consists of a general, a neurological and a neurourological examination, including digital rectal examination, evaluation of sensibility and muscle behavior of different muscle groups, including the pelvic floor muscles, abdominal and thigh muscles. Bulbocavernosus and anal reflex behavior was noted. In case of symptoms in other regions an evaluation of involved muscles, i.e. arm muscles, was carried out. A search for pain trigger points in the abdominal wall and pelvic floor areas was done and if present recorded. All symptoms were proved regarding reproducibility at a second office visit.

A urine analysis was carried out in order to exclude an infection as cause for complaints reported.

Anatomical abnormalities of the kidneys, bladder, uterus/prostate were excluded by ultrasound imaging. A complex videourodynamic evaluation was performed in every patient. This included free uroflowmetry, cystometry, and urethral profilometry.

If necessary further investigations (e.g. computed tomography, magnetic resonance imaging) were undertaken in order to exclude associated pathological changes (e.g. vertebral disc prolapse, organ tumor) as cause for the non-urolological symptoms reported.

Results

Within 12 months, 22 patients (18 women, 4 men; mean age 42 (18–60) years) out of 213 patients with non-neurogenic voiding dysfunction were seen suffering from additional somatic symptoms involving the TMJ, distal forearm/hand, or feet (see Table 1). Lower urinary tract symptoms included urge incontinence in 12 cases, frequency in five cases, retentive voiding habits and chronic urinary retention in three cases. All patients were still under treatment, most taking anticholinergic medication ($n=17$). Pain medication, tricyclic antidepressants and alphablockers are used in only few patients.

Eight patients suffered from a TMJ syndrome with pain in the masseter area, chewing problems, head- and neckache. Skin numbness as a sign of sensory disturbance was seen in one patient with TMJ-syndrome.

Nine patients with lower urinary tract symptoms suffered from upper extremity problems including muscle weakness and arm/elbow pain. Sensory problems were seen in seven patients complaining about dysaesthesia and numbness of the arm/hand skin.

Five patients complained about leg symptoms like pain and muscle weakness, numbness in the leg and sensory deficits.

Headache as a major problem was seen in nine patients with lower urinary tract symptoms independent from problems with extremity or mastication muscles.

In all reviewed cases symptoms of bladder dysfunction emerged first. Significant-associated symptoms were experienced after a medium time interval to the occurrence of lower urinary tract symptoms of 20.8 (1–82) months. Over time changes of bladder symptoms were accompanied by changes of associated symptoms. Successful treatment of bladder problems resulted in relief of associated symptoms whereas aggravation of bladder symptoms was usually followed by grad-

Table 1. Urodynamic data from patients with severe chronic bladder dysfunction and accompanying symptoms (normal: bladder capacity: 400–500 ml; sphincter closure pressure: 60–80 cmH₂O; peak uroflow: 25 ml/s; average uroflow: 12.5 ml/s)

Patient group	Cystometry			Profilometry and uroflowmetry			
	Average bladder capacity (ml)	% Patients with increased bladder sensitivity	% Patients with normal bladder compliance	Average sphincter closure pressure (cmH ₂ O)	Average Peak uroflow (ml/s)	Average medium uroflow (ml/s)	% Patients with abnormal uroflow pattern
Women (<i>n</i> = 18)	369	88.9	83.3	90	16.5	7.1	100
Men (<i>n</i> = 4)	592	75	100	94	12.3	7.3	100
All (<i>n</i> = 22)	414	86.4	86.4	91	15.6	7.1	100
TMJ-syndrome (<i>n</i> = 8)	380	87.5	75	92.5	15.5	6.8	100
Upper extremity problems (<i>n</i> = 8)	501	87.5	87.5	89	15	6.9	100
Lower extremity problems (<i>n</i> = 6)	424	100	100	97.3	20.2	9.2	100

ual change for the worse of the other symptoms as well.

All 22 patients, suffered from a urodynamically-proven voiding and pelvic floor dysfunction. There was a broad variety of urodynamic findings including frequency, urgency, incontinence, chronic urinary retention, weak uroflow, double voiding and residual volumes. Urodynamic data from these patients are summarized in the following Table 1.

Whereas basic parameters of bladder function, i.e. bladder volume and bladder compliance, are within normal ranges, there are increased sensations of bladder filling and increased urethral closure pressures in the majority of patients. Consequently flow parameters, including maximal flow rate and flow pattern are pathologically changed. These data show that there is a combined bladder and pelvic floor dysfunction.

Discussion

The literature is filled with discussions of poorly-understood syndromes of chronic fatigue and pain [10]. These syndromes encompass a collage of seemingly unrelated symptoms, e.g. muscular or limb pain, dysaesthesias, allodynia, sensitization, hyperalgesia, referred pain, headache, TMJ dysfunction, irritable or spastic bowel/bladder, pelvic pain, and emotional disturbances (i.e. depression,

sleep disorders, etc.). Some of these symptoms appear after traumatic injury and are diagnosed as a “reflex sympathetic dystrophy” (RSD) or now based on the new definition as “complex regional pain syndrome” (CRPS) [11, 12]. Furthermore, these symptoms could affect body regions at a distance from the injured or dysfunctional organ [13]. It has now been recognized that these symptoms can occur without traumatic nerve lesion and are sympathetically maintained [14].

After a validation process the criteria of the International Association for the Study of Pain (IASP) for the diagnosis of CRPS are today as follows [15, 16]:

1. continuing pain that is disproportionate to any inciting event;
2. must report at least one symptom in each of the four categories
 - sensory disturbances – hyperaesthesia
 - vasomotoric changes
 - oedema and/or sweating changes
 - decreased range of motion, motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (skin, hair, nail);
3. must display at least one sign in two or more of the following categories
 - evidence of hyperalgesia and/ or allodynia
 - evidence of temperature asymmetry or skin color changes
 - evidence of oedema or sweating changes

- evidence of decreased range of motion or motor dysfunction and/ or trophic changes

These criteria can not be simply adapted to the clinical phenomena reported. However chronic bladder dysfunction may harm nervous tissue at different levels of the CNS via an increased afferent input of sensory and noxious stimuli [2, 17]. Symptoms of CRPS will occur.

Many of the symptoms, experienced by the patients reported in this study were similar to those reported as RSD/CRPS phenomena, and included sensory and distinct motor dysfunction, and varying degrees of vasomotor changes [18, 19]. Traumatic events were excluded. Evolving views of these disorders are now placing greater emphasis on central nervous dysfunction as the cause, and focus of therapy [17]. Although the actual mechanism(s) is/are as yet unknown, it has been demonstrated that neurotransmitter metabolism and cerebral perfusion, are changed [20]. Over a longer time frame, aberrant neural activity can become memorized via alterations in protein synthesis and new synaptic connections [13].

Most interesting was an observed improvement in all symptoms when the voiding dysfunction was successfully treated. Various forms of neuromodulation (biofeedback, acupuncture, α -receptor blockers, external and sacral electrostimulation) have the potential to improve bladder/pelvic floor dysfunction and also associated symptoms. Unfortunately besides of case reports up to now there are no valid scientific data published [21].

The CNS has an inherent tendency to become unstable and the resulting regulatory inefficiencies are reflected in end organ behavioral disturbances (e.g. urinary frequency, pain) [18]. Normal bladder function is possible only through controlled dampening or gating of either input to or output from higher centers within the CNS (e.g. the difference between the infantile and adult bladder) [22]. Deterioration of this CNS capability to modulate bladder function could occur as a result of either a true anatomic pathology (e.g. spinal cord injury) or of some metabolic failure (e.g. change of central transmitter pools, new synaptic branching), with the end result being dysreflexic syndromes similar to those as reported here.

The concept that lower urinary tract dysfunction can be the primary or secondary cause of symptoms in other regions of the body seems far

fetched by traditional clinical and scientific perspectives. The concept is, however, well accepted in the management of spinal cord injury patients (e.g. autonomic dysreflexia). A linkage between “non-neurogenic” lower urinary tract dysfunction and symptoms involving the masseter, hand or foot, is strongly supported by the clinical observations presented. Neuronal plasticity allows the cell and the organism to adapt to its particular ecological or behavioral niche. It is of evolutionary importance because it provides the means by which an organism can continuously adapt to its environment [23, 24]. However, plasticity does not guarantee that all change will be for the comfort and well-being of the patient. Complaints and functional diseases may occur.

It follows that medical inquiry into lower urinary tract dysfunction should include all symptoms affecting quality of life. If there are specific complaints associated to lower urinary tract dysfunction a neurological exam should be performed that includes assessment of skin temperature and sensitivity, extremity reflexes and motor power, i.e., hand grip, balance etc. Therapy that focuses on the urinary tract could bring about significant improvement in associated symptoms.

References

1. Erickson DR, Morgan KC, Ordille S, Keay SK, Xie SX. Nonbladder related symptoms in patients with interstitial cystitis. *J Urol* 2001; 166: 557–561.
2. Zermann DH, Ishigooka M, Deggweiler R, Schmidt RA. Neurourological insights into the etiology of genitourinary pain in men. *J Urol* 1999; 161: 903–908.
3. Head H, Riddoch G. The automatic bladder, excessive sweating and some other reflex conditions, in gross injuries of the spinal cord. *Brain* 1917; 40: 188–263.
4. Trop CS, Bennett CJ. Autonomic dysreflexia and its urological implications: a review. *J Urol* 1991; 146: 1461–1469.
5. Vaidyanathan S, Soni BM, Sett P, Watt JW, Oo T, Bingley J. Pathophysiology of autonomic dysreflexia: long-term treatment with terazosin in adult and pediatric spinal cord injury patients manifesting dysreflexic episodes. *Spinal Cord* 1998; 36: 761–770.
6. Guttmann L, Whitteridge. Effects of bladder distension on autonomic mechanism after spinal cord injuries. *Brain* 1947; 70: 361–404.
7. Linsenmeyer TA, Campagnolo DI, Chou IH. Silent autonomic dysreflexia during voiding in men with spinal cord injuries. *J Urol* 1996; 155: 519–522.
8. Bannister R, Oppenheimer DR. Degenerative diseases of the nervous system associated with autonomic failure. *Brain* 1972; 95: 457–474.

9. Groutz A, Blaivas JG, Pies C, Sassone AM. Learned voiding dysfunction (non-neurogenic, neurogenic bladder) among adults. *Neurourol Urodyn* 2001; 20: 259–268.
10. Suhr JA. Neuropsychological impairment in fibromyalgia. Relation to depression, fatigue, and pain. *J Psychosom Res* 2003; 55: 321–329.
11. Wilson PR. Complex regional pain syndrome – reflex sympathetic dystrophy. *Curr Treat Options Neurol* 1999; 5: 466–472.
12. Turner-Stokes L. Reflex sympathetic dystrophy – a complex regional pain syndrome. *Disabil Rehabil* 2002; 24: 939–947.
13. McMahon SB, Wall PD. Receptive field of lamina I projections cells move to incorporate a nearby region of injury. *Pain* 1984; 19: 235–247.
14. Stanton-Hicks M, Jänig W, Hasenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain* 1995; 63: 127–133.
15. Bruhl S, Harden RN, Galer BS et al. External Validation of IASP diagnostic criteria for complex regional pain syndrome and proposed research diagnostic criteria. *Pain* 1999; 81: 147–154.
16. Harden RN, Bruhl S, Galer B et al. Complex regional pain syndrome: are the IASP diagnostic criteria valid and sufficiently comprehensive? *Pain* 1999; 83: 211–219.
17. Janicki TI. Chronic pelvic pain as a form of complex regional pain syndrome. *Clin Obstet Gynecol* 2003; 46: 797–803.
18. Jänig W. Relationship between pain and autonomic phenomena in headache and other pain conditions. *Cephalgia* 2003; 23: 43–48.
19. Harden N. Complex regional pain syndrome. *Br J Anaesth* 2001; 87: 99–106.
20. Goldenberg DL. Fibromyalgia, chronic fatigue syndrome, and myofascial pain. *Curr Opin Rheumatol* 1996; 8: 113–123.
21. Zermann DH, Weirich T, Wunderlich H, Reichelt O, Schubert J. Sacral nerve stimulation for pain relief in interstitial cystitis. *Urol Int* 2000; 65: 120–121.
22. Schmidt RA, Zermann DH, Deggweiler R. Urge incontinence update: old traditions and new concepts. *Adv Intern Med* 1999; 44: 19–57.
23. Strittmatter SM, Vartanian T, Fishman MC. GAP-43 as a plasticity protein in neuronal form and repair. *J Neurobiol* 1992; 23: 507–520.
- 24.Coderre TJ, Katz J, Vaccarino AL, Melzack R. Contribution of central neuroplasticity to pathological pain: a review of clinical and experimental evidence. *Pain* 1993; 52: 259–285.

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