Paraplegia 18 (1980) 221-225 0031-1758/80/01030221$02.00

Proceedings of the Annual Scientific Meeting of the International Medical Society of Paraplegia held in Mulhouse, France, in July 1979

THE NEUROPATHIC URETHRA

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Abstract. The hypothesis is advanced that the functional urethral obstruction found in neuropathic states is due, in part at least, to urethral supersensitivity following sympathetic decentralisation.

A simple postural test for this condition is described. By its use it has been shown that urethral denervation occurs not only in disorders of the central nervous system but with peripheral damage such as may result from rectal excision and hysterectomy.

In some cases with functional urethral obstruction, attributable to supersensitivity of the urethra, no neurological abnormality has been found. These may be examples of localised visceral neuropathy.

Key words: Neuropathic urethra; Urethral supersensitivity test; Urethral obstruction.

BLADDER function reflects the relationship between intravesical pressure and urethral resistance. In disorders of the nervous system poor bladder emptying is more often due to urethral obstruction than to subnormal voiding pressures. The bladder, however, was almost exclusively the focus of attention in these cases until less than 50 years ago. Then Watkins (1936) reported finding obstruction at the level of the membranous urethra in patients with lesions of the sacral segments. Internal membranous urethrotomy (loosely called 'external sphincterotomy') was introduced for the relief of these cases (Ross *et al.*, 1957), and whilst it proved effective, the mechanism of the obstruction was obscure (Gibbon, 1973).

About the same time Emmett *et al.* (1948) noted the common occurrence of membranous urethral obstruction in spastic paraplegics and suggested its relief by subarachnoid alcohol block, sacral rhizotomy or pudendal neurectomy on the assumption that contraction of the striated muscle of the urethra or pelvic floor was responsible. Electromyography has given some support to this concept (Diokno *et al.*, 1974). Rhizotomy, whether chemical or surgical, gave effective relief and the accompanying loss of reflex bladder activity could be compensated for, except in cervical lesions, by abdominal straining or manual compression. Unfortunately, the inevitable impotence produced by sacral rhizotomy was unacceptable to many patients, and pudendal neurectomy as an alternative therefore had a vogue. This operation proved unreliable, however, which is not surprising in view of the repeated demonstration that the internal pudendal nerves do not supply the external urethral sphincter (Gil-Vernet, 1964; Donker *et al.*, 1976). On the other hand, impotence was an unexpectedly common complication and one which has not even yet been adequately explained. Internal membranous urethrotomy, aimed at dividing the striated urethral sphincter, has now become firmly established as the procedure of choice for these cases (Ross *et al.*, 1976) as well as for the sacral segment cases for whom the operation was originally described.

The mechanism of neuropathic urethral obstruction, particularly in conus

lesions, has been the subject of research at Southport for the past 30 years. An obvious clue was the traditional belief that some paraplegics void more easily lying down that when sitting, and so the retrograde urethral resistance was measured in a series of paraplegics in the two positions. Assumption of the upright posture was associated with a marked increase of resistance in most of these patients whatever the level of the spinal lesion (Gibbon, 1973). The introduction of urethral pressure profilometry enabled the wall pressure along the urethra to be shown graphically and fresh light was soon shed on the problem by Donker's (1972) demonstration that in the normal subject a major part of the peak urethral resistance (at the level of the urogenital diaphragm) is due to muscle under alpha-adrenergic control. Following this clue we obtained urethral pressure profiles in the supine and sitting positions before and after the administration of an alpha-blocking agent in two patients with sacral lesions (Abel *et al.*, 1974). Sitting up was associated with an abnormal increase in the peak pressure while an alpha-blocking agent flattened the curve in both positions.

Assessments of the alpha-adrenergic contribution to the peak of the urethral pressure profile and the effect of posture were then made in 42 spinal injury cases, six of whom had had an unsuccessful internal membranous urethrotomy, and the findings compared with 16 normal subjects (Shamsunder *et al.*, 1978). A normal or excessive alpha-adrenergically innervated muscular component of urethral pressure was found whatever the level of the cord lesion excluding the region of the thoraco-lumbar junction from which emerges the sympathetic outflow to the bladder and urethra. Furthermore, a significant positive postural response was found in all the patients with neurological lesions of or below T11. In eight of these cases tested with an alpha-adrenergic blocking agent, all or part of the increase was abolished by the drug. The postural effect was particularly striking when the cord segments T11–L2 were involved without loss of the sacral reflex arcs. The next greatest response was seen in the three sacral lesions with apparently intact efferent sympathetic pathways. In the six failed urethrotomy cases a marked postural response was found, most of which was abolished by an alpha-blocker. These were all cases with supra-sacral lesions and the implication was that in such patients not all the abnormal urethral resistance is due to striated muscle under somatic control.

We then investigated a series of paraplegics and general urological cases along the same lines but in addition, following a suggestion from Professor G. Brindley, pneumatic thigh cuffs were used in the supine position to simulate the haemodynamic changes associated with a change to the upright position. Sympathetic decentralisation of the urethra was found to be associated with an abnormal postural response, and this could be reproduced accurately by the application of thigh cuffs in the supine position provided that there was not excessive wasting of the legs. These findings were thought to support a humoral rather than a reflex mechanism for the urethral behaviour (Parsons and Turton—1980), and form the basis of a simple test for the diagnosis of adrenergic supersensitivity of the urethra.

Supersensitivity of denervated muscle to chemical agents was first described in 1905 by Elliott in relation to the iris. It is well known to urologists who use the Lapides Test for denervation of the bladder. This involves injecting a cholinergic drug subcutaneously, and monitoring the subsequent change in bladder pressure. One of the attractions of the test which we have developed for urethral decentralisation is that a simple modification of posture or venous return is used to induce the desired humoral stimulus (*i.e.* an increase in the level of circulating catecholamines) so excluding the need for exogenous stimulation. However, the urethral super-

sensitivity concept is also supported by the results of intravenous injection of alpha-adrenergics (Koyanagi, 1979). The poor postural response in high lesions is no doubt due to impaired homeostasis (Guttmann *et al.*, 1963).

The new test has been applied to selected cases undergoing urethral profilometry and several groups of patients showing a positive response have been identified.

1. *Patients who have had abdomino-perineal excision of the rectum.* A prospective study of 43 cases showed the bladder to be partially or completely denervated in 23, as evidenced by an early positive Lapides Test and later (after three months) a hypertonic filling cystometrogram with areflexia. In 11 of these 23 cases with a paralysed bladder, detailed studies of the urethra were done. Urethral adrenergic supersensitivity was found in seven of these cases, all of whom were found to be obstructed in the region of the membranous urethra (Parsons—in preparation).

2. *Patients with an obstructed void after hysterectomy.* In the five years 1973–78, 208 women were referred to our urodynamic clinic with urinary symptoms. Eighty-nine showed an obstructed void, and of these over a third had had a hysterectomy, an incidence three times that found among the non-obstructed cases. The suspected association between hysterectomy and urethral obstruction is confirmed by an analysis of the 48 cases in which the uterus had been removed. More than two-thirds of these patients showed a functional urethral obstruction, whereas only about one-third of the non-hysterectomy cases were so affected. Eighteen patients presenting with urinary symptoms after hysterectomy have now been fully investigated with urethral profilometry in different postures before and after alpha blockade, and by voiding cysto-urethrography. Of these, 15 showed clear evidence of urethral denervation supersensitivity and 13 were obstructed. The remaining three had unobstructed voids (Woolfenden *et al.*—in preparation). A prospective study is now under way to establish the incidence and importance of this functional urethral obstruction which may actually be advantageous in some cases of stress incontinence. It is often claimed that when a hysterectomy is combined with an anterior vaginal repair for stress leakage the results are significantly improved. Urethral denervation could produce an explanation of this experience. Furthermore, the repair itself could denervate the urethra in some cases with beneficial effect. It may be significant that simple vesico-urethrolysis is said to give as high a rate of cure as a formal repair (Mulvaney, 1951). Further investigation of these problems may well be of practical importance.

3. *Occult urethral neuropathy.* Evidence of decentralisation of the urethra has been found in four patients without any obvious neurological abnormality. These include one elderly male following the removal of a large prostate which might conceivably have caused derangement of the sympathetic innervation of the posterior urethra. The three other cases were all women, none of whom had undergone hysterectomy or vaginal repair. Each case showed identical urethral responses and it was speculated that they may have an occult urethral neuropathy (Parsons and Turton, 1980).

Discussion

The concept of the neuropathic urethra is clearly full of potential in both theoretical and practical terms. It may be important that we give greater emphasis

in future to functional rather than anatomical concepts. For example, the peak of the urethral pressure profile may well be largely due to the striated external urethral sphincter but this may be influenced to varying degrees by a sympathetic and a somatic innervation (El Badawi and Schenk, 1974) according to circumstances.

It is interesting that urethral supersensitivity develops not only in cord lesions and with damage to the pelvic plexuses, but also when the conus is involved. This lends some support to the proposition that the intermediate sympathetic neurones originate not only from the segments traditionally implicated (T1–L2) but also from the sacral segments themselves. These neurones are said to travel up the cord to be distributed with the white rami in the usual way. (Laruelle, 1937, 1948). An alternative explanation could be based on the work of Elbadawi and Schenk (1974), who believe that the striated urethral sphincter has a triple nerve supply influencing the final common pathway, and that sympathetic and parasympathetic influences modulate one another. On this view, damage to the conus would leave the sympathetic innervation intact but in an overactive state due to withdrawal of the cholinergic impulses. The findings in true cauda equina lesions should enable us to differentiate between these two hypotheses. So far, two such cases have been investigated fully, and in both there was no evidence of urethral supersensitivity, which would support Laruelle's anatomical findings.

Conclusion

From the practical point of view, it seems clear that in the investigation of voiding problems whether in normal or neuropathic cases, measurement of the urethral resistance in the supine position alone is of limited value. The new test for urethral supersensitivity described here should prove helpful in the investigation of problem cases as well as in basic urodynamic research.

Whilst alpha-adrenergically innervated muscle (which probably includes the striated sphincter) is of great importance in vesico-urethral neuropathy, the results of oral alpha-blocking therapy for the relief of urethral obstruction have been, in our experience, disappointing. It is possible that the supersensitive muscle once blocked alters its sensitivity, and thus a variety of alpha-blockers would be required for continuous relaxation of the urethra. Unfortunately we also find that the scope of this therapy is seriously limited by the side-effects among which nasal congestion seems to be even more important than postural hypotension. Operative intervention, however, is now both safe and effective and for long-term benefit urethrotomy is probably preferable to drug therapy. Internal membranous urethrotomy may be more widely used when it is realised that the procedure does not cause stress incontinence provided that the bladder neck remains intact. Finally, a sound rationale can now be proposed for the selective treatment of vesico-urethral neuropathy based on full urodynamic investigation rather than the empirical approach whereby urethrotomy is done only when bladder-neck resection fails.

Summary

1. The functional urethral obstruction found in neuropathic states has been shown to be related to posture and to be wholly or partly due to alpha-adrenergically innervated muscle.

2. Evidence is presented for the hypothesis that decentralisation supersensitivity of the urethral muscle plays an important part in this type of dysfunction.

3. A simple test for urethral supersensitivity is described.

RÉSUMÉ

1. L'obstruction fonctionnelle de l'uréthre qu'on trouve à l'état neuropathique est, selon les dernières observations, en rapport avec la posture et resulte entièrement ou partiellement de muscle alphadrenergicalement ennervé.

2. On présente des observations à l'appui de l'hypothèse selon laquelle l'hypersensibilité décentralisée du muscle uréthral joue un rôle important dans les dysfonctions de ce genre.

3. On décrit un procédé relativement simple pour dépister l'hypersensibilité uréthrale.

ZUSAMMENFASSUNG

1. Wir haben gezeigt, dass die funktionelle Obstruktion der Urethra die man in Neuropathien findet, mit der Körperhaltung verbunden ist. Ganz oder teilweise ist sie auf alphaadrenergische innervierte Muskeln zurück zu fuehren.

2. Warscheinlich spielt 'Dezentralisation Hyper-Sensibilität' eine wichtige Rolle in diesem Typus der Dysfunktion.

3. Eine einfache Untersuchung für Hyper-Sensibilität der Urethra wird beschrieben.

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