

URINARY INCONTINENCE CAUSED BY PRAZOSIN

Dear Sir,

In the article on "Urinary incontinence caused by prazosin" by Rachagan and Mathews⁽¹⁾ stated that the urinary incontinence in a 62-year-old menopausal female treated with prazosin is due to its action as an alpha adrenoreceptor blocker, since urethral closure is mediated by sympathetic alpha adrenoreceptor activity which causes the smooth muscles of the proximal urethra (PU) to contract (see their Fig 1).

However, the female anatomy, in particular, lacks a smooth muscle sphincter in the wall of the bladder neck and proximal urethra⁽²⁾. It would be difficult to perceive proximal urethra smooth muscle contraction maintaining urinary continence in females when they do not have such a sphincter. Obstruction of the bladder neck in females is practically unknown. Recognising this anatomical fact in females, Dixon and Gosling⁽³⁾ stated that active smooth muscle contraction cannot be an important factor in the continence of urine in women. In males where an anatomical smooth muscle sphincter is present in the proximal urethra (pre-prostatic), the sympathetic induced sphincteric closure is a 'genital sphincter' with a sexual role associated with preventing retrograde flow of semen into the urinary bladder at ejaculation rather than with urinary continence^(2,3). Surgical sectioning of hypogastric nerves or radical sympathectomy for various conditions, including the relief of pain or hypertension, had no effect on micturition^(2,4).

Alpha-1 adrenoreceptor agonists as well as antagonists administered directly on spinal nerves via intrathecal (i.t.) injections produced no effect on volume-evoked micturition reflexes⁽⁵⁾. Prazosin is an alpha-1 adrenoreceptor antagonist.

The early perception that sympathetic nerves are the 'filling' nerves of the bladder and that the parasympathetic nerves are concerned with the 'emptying' of the viscus, has been refuted⁽⁶⁾. The reflex integration of bladder and sphincteric function is exemplified by the seven Barrington's micturition reflexes. Except for the 3rd Barrington's reflex, (viz stimulation by urethral distension producing a small degree of bladder contraction response), sympathetic hypogastric nerves are not implicated at all⁽⁷⁾.

Besides spinal level regulation, there are discrete sprasinal micturition centres, eg, the pontine micturition centre or PMC comprising of locus coeruleus, lateral tegmental nucleus, and periaqueductal nuclei where the first two, viz locus coeruleus

and the lateral tegmental nucleus, contain noradrenergic neurons. The locus coeruleus is also known as a noradrenaline center in the brain. Noradrenaline modulates the activity of preganglionic parasympathetic neurons⁽⁷⁾ and intrathecal injection of prazosin has been shown by Yoshimura et al⁽⁸⁾ to cause blockage of locus coeruleus-initiated bladder contractions in rats with resected hypogastric nerves. Apparently then, prazosin has a definite effect in central pathways of micturition regulation. Incomplete interruption (since only 2 out of 3 nuclei groups in the pontine micturition centre have noradrenaline neurons) might lead to an unstable bladder or enuresis. Enuresis occurs naturally in infancy but gets stabilized with maturity, possibly from better developed supraspinal control.

In view of the documented experimental evidence regarding a positive prazosin effect in supraspinally motivated micturition response, but no effect from similar antagonism when the micturition reflex was evoked at spinal level, it seems likely that the observed prazosin-induced urinary incontinence could be a supraspinal effect rather than a direct spinal level neurogenic response. As observed earlier, there are definite anatomical, surgical and pharmacological difficulties in perceiving a spinal level prazosin effect.

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ANSWER TO ELECTROCARDIOGRAPHIC CASE

DIAGNOSIS:

Fig 1: Complete heart block with prolonged QT interval

Fig 2: Torsades de pointes

DISCUSSION

The ECG in Fig 1 shows complete heart block with a ventricular rate of 48 beats/minute. The QT interval was prolonged at 539 msec (QTc 506 msec), and associated with a prominent U wave. At the time of the patient's giddiness, the ECG revealed multiple episodes of non-sustained polymorphic ventricular tachycardia. The ECG in Fig 2 shows polymorphic ventricular tachycardia triggered by an 'R on T' and aborted later with a precordial thump. This rhythm is consistent with a diagnosis of torsades de pointes.

Torsades de pointes (French translation : "twisting of the points") is a form of ventricular tachycardia diagnosed on the following morphologic criteria :

1. a ventricular rate of >200/minute.
2. QRS morphology displaying alternating polarity in an undulating pattern giving an appearance of complexes twisting around the baseline.
3. the arrhythmia is typically non-sustained.

Some authors include QT prolongation (>500 msec) and 'R on T' phenomenon as additional diagnostic criteria⁽¹⁻³⁾. It was originally described in the setting of bradycardia due to complete heart block. The arrhythmia received its present name from Dessertenne in 1966⁽⁴⁾ although it had been described previously by MacWilliams⁽⁵⁾ and Wiggers⁽⁶⁾. It is frequently regarded as intermediate between ventricular tachycardia and ventricular fibrillation.

Its mechanism is partially understood. The prolonged QT interval (a reflection of prolonged repolarization) reflects temporal dispersion of ventricular refractory periods, predisposing to multiple reentry⁽⁷⁾. Alternatively, afterdepolarization, either early (EADs) or delayed (DADs), have been suggested as likely mechanisms⁽⁸⁾. The lengthened QT interval also increases the duration of the vulnerable period during which additional stimuli can provoke ventricular tachycardia or ventricular fibrillation. It also shortens the diastolic period, decreasing the degree of prematurity needed for a premature beat to fall within the vulnerable period⁽⁹⁾.

Although torsades de pointes is typically non-sustained because the electrophysiologic heterogeneity is not sufficient to maintain a continuous fibrillatory process⁽¹⁰⁾, there are times when it can degenerate into ventricular fibrillation or

spontaneously transform into ventricular tachycardia or flutter.

The association between marked QT prolongation and torsades de pointes may be congenital or acquired. Significant differences exist between the two, most notably in their relation to the sympathetic nervous system⁽¹¹⁾. In the congenital form, torsades de pointes usually develops during exertion or emotional stress and is exacerbated by beta-adrenergic agonists (adrenergic-dependent). Prolonged full-dose beta-blocker therapy has been shown to be of benefit in this subgroup of patients⁽¹²⁾ but when this fails, left cardiac sympathetic denervation should be considered⁽¹³⁾. In the acquired type, torsades de pointes is precipitated by long ventricular cycles or pauses and is usually not related to exercise or emotional stress (pause-dependent). Apart from eliminating the underlying cause, pacing is the most effective therapy in this patient subgroup.

The patient described had no reversible causes for her prolonged QT interval. As she had a history of cardiac arrest and documented ventricular arrhythmia at the time of her giddiness, she was implanted with a pacemaker (Fig 3). She has since remained well.

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