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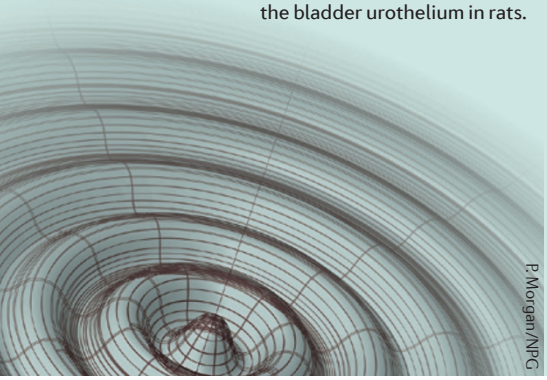
URINARY INCONTINENCE

Shock waves enable BoNT-A uptake by urothelium

Intravesical injections of onabotulinum toxin-A (BoNT-A) are widely used in the management of bladder overactivity that is refractory to more conservative treatments. Now, findings of basic research have identified a method of delivering BoNT-A to the bladder, without the need for intravesical injections.

Researchers used low-energy shock waves (LESW), delivered through the skin area over the bladder dome to temporarily permeabilize the bladder urothelium in rats.



P. Morgan/NPG

Commenting on the rationale for this approach, lead author Yao-Chi Chuang explains "low-energy shock waves have been shown elsewhere to temporarily increase tissue permeability" adding that "these shock waves can enable the delivery of molecules of up to 2MDa into the cytoplasm of cells, without toxicity". Indeed, no significant toxic effects of LESW on rat bladders were identified 1 hour post-treatment.

The induction of permeability following LESW was initially confirmed using contrast enhanced MRI; furthermore, a shock intensity of 0.10–0.13 mJ/mm^2, delivered as 200–300 impulses was found to be optimal.

In order to test whether BoNT-A could be delivered to the urothelium in such a way, and whether or not this would be effective, researchers used acetic acid instillations, which reduced the intercontraction intervals by around 70%. However, in rats pretreated with LESW plus intravesical instillation of BoNT-A, acetic acid instillations were significantly less effective at reducing the intercontraction interval, suggesting that BoNT-A delivered using this method can attenuate bladder overactivity. Furthermore, BoNT-A delivered in this way resulted in decreased inflammation, and reduced SNAP-23 and COX-2 expression compared with saline, LESW or BoNT-A-treated controls.

Summarizing these findings, Chuang concludes "LESW can facilitate delivery of BoNT-A without significant bladder toxicity". When asked about the clinical relevance of this research, Chuang adds "Intravesical injections of BoNT-A into the bladder are effective; although, certain risks exist, such as haematuria, pain and UTI." Thus, this approach might provide an alternative to intravesical injections, which could be welcomed by patients that require repeat injections of BoNT-A in order to manage their symptoms.

When asked about future directions, the authors note that these findings, although promising, cannot be extrapolated directly to human patients, adding that data from dose-adjusted proof-of-concept studies would be an important step towards clinical implementation.

Peter Sidaway

ORIGINAL ARTICLE Chuang, Y. C. *et al.* Urodynamic and immunohistochemical evaluation of intravesical botulinum toxin A delivery using low energy shock wave. *J. Urol.* http://dx.doi.org/10.1016/j.juro.2015.12.078 (2015)

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