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Does Cutaneous Stimulation of the Peroneal Nerve Treat Overactive Bladder?

Overactive bladder (OAB) is well studied not only on its clinical and economic importance, but also for its unique barriers to adequate treatment. Though AUA/SUFU (Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction) guidelines recommend a sequential treatment algorithm of increasing invasiveness, it is understood that over 66% of patients fail first-line therapy (ie, behavioral modifications),[1] and over 53% lack adherence to second-line therapy (ie, medical therapy).[2-4] Despite this, only a fraction of patients (2.7%-3.9%) proceed with third-line therapy (ie, surgical interventions).[5] These high attrition rates have been attributed to poor patient education, medical therapy side effects, perceived invasiveness of third-line therapies, and cumulative costs of treatments.[6,7] For all the above reasons, the option for a noninvasive therapy with minimal side effects is highly desirable.

Typical nerve targets for OAB include sacral, pudendal, and tibial. Both animal and human studies exist showing inhibition of detrusor overactivity with stimulation of these nerves. This study by Krhut et al (page 734) is targeting the peroneal nerve in hopes of improving OAB symptoms.[8] The common peroneal nerve (L4-S2) is a terminal branch of the sciatic nerve and carries both sensory and motor components. It courses along the upper, lateral side of the popliteal fossa and can be palpated behind the head of the fibula as it courses down to innervate the dorsum of the foot. The superficial nature of this nerve makes it accessible to cutaneous stimulation. However, what is lacking is clear evidence that stimulation of the peroneal nerve inhibits bladder activity. For instance, Yu et al utilized a cat model to show that peroneal nerve stimulation led to an excitatory reflex in the bladder, whereas the tibial nerve resulted in bladder inhibition.[9] Despite an increase in bladder capacity after tibial nerve stimulation by 140.5%±7.6% of the control capacity, subsequent peroneal nerve stimulation restored the bladder capacity and increased contractions by 200%. The authors hypothesized that "The superficial peroneal nerve and tibial nerve innervate the dorsal and plantar surfaces of the foot and elicit opposite motor responses, producing dorsiflexion and plantar flexion of the foot, respectively. Therefore, it is possible that the dorsiflexion/plantar flexion induced by [peroneal nerve stimulation/tibial nerve stimulation] or the afferent firing that induces these flexor and extensor reflexes has opposite effects on the bladder." Therefore, the authors suggested that peroneal nerve stimulation may be a target for underactive, not overactive, bladder.

Strong clinical data on humans are lacking. A study by Hare et al suggests that peroneal nerve stimulation can improve scores on the ICIQ-OAB (International Consultation on Incontinence Questionnaire Overactive Bladder Module) in patients with multiple sclerosis ($P = .043$), though not within the entire cohort of those with other neurological disorders.[10]

In this multicenter, prospective randomized study of transcutaneous neuromodulation of the peroneal nerve (eTNM) compared to daily solifenacin, the authors reported an excellent safety profile of mostly transient erythema and mild pain at site of stimulation for the former compared to dry mouth and constipation for the latter. Treatment adherence was comparable between the 2 cohorts. Clinical efficacy was a secondary objective, and thus the study was not adequately powered. In general, comparing all the objective and subjective outcomes, there were no differences between groups. Of interest, the solifenacin group had a more rapid onset of symptom improvement than the eTNM group despite daily use of the device.

The authors should be commended for seeking a minimally invasive neuromodulation target that can be used at home to improve OAB symptoms. This study suggests that the peroneal nerve may be that target. However, given the conflicting data seen in animal studies and the known placebo effect associated with neuromodulation, either a sham-controlled trial by choosing an alternative electrode placement on the lower extremity or a randomized trial comparing posterior tibial nerve

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stimulation to eTNM of the peroneal nerve would help elucidate, and perhaps solidify, the authors' findings. This would give the clinician confidence that modulating the peroneal nerve is effective for the treatment of OAB.

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