Transcutaneous electric nerve stimulation (TENS) for the treatment of nocturnal enuresis in children

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Objectives
1. To review treatment options for monosymptomatic nocturnal enuresis
2. To improve understanding of how neuromodulation improves various voiding dysfunctions
3. To learn about how TENS therapy can be used to help treat patients with nocturnal enuresis

Abbreviations
DDAVP - desmopressin
OAB - overactive bladder
OSA - obstructive sleep apnea
PIN-Q - pediatric urinary incontinence quality of life
PNE - primary monosymptomatic nocturnal enuresis
PS - parasacral
PTNS - posterior tibial nerve stimulation
SP - suprapubic
TENS - transcutaneous electric nerve stimulation
UTI - urinary tract infection

No Disclosures
No Conflicts of Interest
Overview

- Nocturnal enuresis
- Neuromodulation in Urology
  - Interstim
  - PTNS
  - TENS therapy
  - Safety
  - Previous Studies
- Our studies

Nocturnal Enuresis

- Bedwetting
- A common problem in pediatrics
- Many causes
  - Primary: patient has not yet had a prolonged dry-night period
    - Developmental delay in nocturnal bladder control in the absence of neurogenic bladder or anatomic anomalies
  - Secondary: wetting again after having stayed dry
    - Examples: stress, UTI, medical condition (e.g., OSA), or side effect of medication (e.g., Lithium)

Nocturnal Enuresis: Treatment Options

- 1. Behavioral Therapy: restrict fluids (especially those high in sugar and caffeine) 2 hours prior to bed, double voiding prior to bed, managed bowel habits, positive reinforcement and allowing child to participate in clean-ups
  - 15-20% effectiveness at achieving dryness
  - More effective in patients <3 years
- 2. Bedwetting Alarm: clip to underwear, loud sound when senses moisture, conditions child to wake at sensation of full bladder
  - 13x more likely to be dry at night if used properly
  - High relapse rate

*Does not work for heavy sleepers (most kids), in my experience*

Nocturnal Enuresis: Treatment Options

- 3. Pharmacologic
  - DDAVP (desmopressin)
    - synthetic ADH
    - Reduces urine production during sleep
    - 4.5x more likely to stay dry
    - More effective in high volume voiders
    - Risk of hyponatremia and seizures
  - Tricyclic antidepressants
    - amitriptyline, imipramine, nortriptyline
    - 4.2x more likely to stay dry
    - Relapse rates 50% after stopping
    - Increased risk of side effects including death from overdose
Neuromodulation

- Alteration of nerve activity by delivering electrical or pharmaceutical agents directly to target areas of the nervous system...to reestablish normal neural balance and improve neural function.
  - *International Modulation Society*

Neuromodulation

- Chronic pain disorders
- Epilepsy
- Migraines
- Spinal Cord Injuries
- Parkinson disease
- Psychiatric (depression, OCD, Tourette syndrome)
- Hypertension
- GI dysmotility
- Fecal Incontinence
- Urinary Incontinence
- Urinary Retention

Neuromodulation in Urology

- Indications:
  - Overactive Bladder (refractory)
  - Urinary Retention (nonobstructive)

- Therapies:
  - InterStim ®
  - PTNS
Based off of main meridian channels of the body

Sites used in nocturnal enuresis or voiding dysfunction treatment:
- Posterior tibial nerve: KI-3, KI-7, KI-10, SP-3, SP-6
- Suprapubic region: CV-2, CV-3, CV-4
- Parasacal: BL-23, BL-28

Acupuncture

- Sacral neuromodulation
  - Technique based on mild electrical stimulation of the pelvic nerves (S3 nerve root) via centrally-located electrodes placed in the sacral foram

InterStim ®

- Involves 2 staged surgeries:
  1st: Test phase (OR or office procedure in adults)
  2nd: Implantation phase (OR)
Posterior Tibial Nerve Stimulation

- Less invasive than InterStim
- Electrode inserted into the posterior tibial nerve at the medial malleolus of the ankle
- Time consuming: 30 min weekly treatment sessions in the clinic for at least 12 weeks

So, if behavioral therapies and medications do not work, the next step is:

1. Trips to the clinic to get a needle put in you every week?
2. 2-stage surgeries with an implant device put in your back?
3. Surgery every 3-6 months (Botox injections during cystoscopy)?

There has GOT to be a better solution...

TENS Therapy

- Transcutaneous Electrical Nerve Stimulation
- FDA approved
- Commonly used for pain disorders and concomitantly during physical therapy for musculoskeletal rehabilitation
- Can be used safely at home

Cons of TENS Therapy

- Adverse warnings: skin irritation and pain
  - Can be managed with proper hygiene, decreasing the intensity, and periodically removing the pads
- Contraindications to use:
  - other implantable devices (eg, pacemaker)
  - submersion in water
  - allergy to electrode, gel, tape
  - pregnancy
  - seizures
  - lymphedema
  - bleeding & clotting disorders
  - impaired cognition
  - cannot place over eyes, anterior neck (carotid sinus), dermatologic lesions, and malignancy
Review of 17 pts with recurrent OAB after daily posterior tibial TENS for 20 min at 10 Hz
- 94% symptomatic improvement at 1 month
- Average length of treatment – 1 month
- At end of treatment, 70% cured without relapse within 9 months
  - 18% with partial improvement
- No side effects

21 parasacral TENS vs 16 sham (scapula) pts with refractory OAB
- Total of 20 sessions, 3x/week, 20 min, 10 Hz
- Reported improvement: TENS 62%, sham 0%
- Reported cure: TENS 57%, sham 0%
- Voided volumes increased with decrease voids/day in TENS

Prospective
- Pts with urgency and diurnal incontinence
- 37 parasacral TENS vs 22 percutaneous PTNS
- Complete resolution of symptoms on 70% of sacral TENS vs 9% of PTNS*
- Frequency of persistence of urgency and diurnal incontinence double in PTNS vs sacral TENS*
  *results not significantly different
Acupuncture in 125 vs DDAVP in 125
- Daily for 15 days (1 session) x 3 sessions
- Evaluation at 2 months
- Total effective rate:
  - 97% acupuncture
  - 90% DDAVP
- Acupuncture more effective than DDAVP for wet nights, onset of therapy, and duration of effect

23 pts with behavioral therapy vs 22 pts with behavioral therapy + parasacral TENS
- 3 sessions/week in the clinic for 20 min at 10 Hz, 10 sessions total
- Rate of wet nights 77% in control and 78% in TENS pre-treatment
- Rate of wet nights 50% in control and 31% in TENS post-treatment
- Average rate of improvement greater in TENS
- No relation to age or gender
- No patient had complete resolution of symptoms

22 patients, mean age 11.4 (7-16) years
- 6 weeks total. Voiding diaries: 2 week pre-stimulation, 2 weeks stimulation, 2 weeks post-stimulation
- Tibial nerve TENS stimulation for 60 min each night
- Mean total wet nights (out of 14):
  - Pre – 9.0 (+/- 4.0)
  - Stim – 6.8 (+/- 4.8)
  - Post – 7.2 (+/- 5.0)
- 73% (16) patients showed improvement of at least 1 less wet night
- No adverse events

There are no studies dealing with ANY pediatric voiding dysfunction (OAB or NE) that have looked compared parasacral, posterior tibial, and suprapubic TENS head-to-head!
TENS for Nocturnal Enuresis

Goals of our study

- To determine if TENS can be offered as an effective and durable at-home therapeutic option for nocturnal enuresis in children.
- To determine which location on the body is optimal for TENS therapy in nocturnal enuresis.

Inclusion criteria

- Presenting with primary monosymptomatic nocturnal enuresis
  - On average more than once per week
- Ages 5-18 years old
- Patients and parents have ability to provide informed consent and complete the study requirements
Exclusion criteria

- Use of pharmacologic or other therapy for urologic disorders in the past 30 days
- Daytime incontinence symptoms
- Wet nights on average once a week or less
- Taking meds predisposing to incontinence (eg, Lithium)
- Other known voiding or neurologic disorders (eg, interstitial cystitis, urinary fistula, myelomeningocele)
- Secondary etiologies (cystitis, obstructive sleep apnea, overactive bladder)
- Any contraindications to TENS
- Prior TENS or neuromodulation

Initial clinic visit

- Day 0
- Recruitment: patients screened and selected for enrollment into the study
- PIN-Q questionnaire
- Behavior techniques taught
- Constipation treated
- Informed consent obtained
- Provided with voiding diaries

PIN-Q survey

- Pediatric urinary incontinence Quality of life tool
- Quantifies the holistic effect of bladder dysfunction in children
- 27 questions in 7 domains:
  - Social relations with peers
  - Self-esteem
  - Family and home
  - Body image
  - Independence
  - Mental health
  - Treatment
- Tested for validity

voiding diary example
Month 1 voiding diaries

- Daily/nightly
- Records each episode of wet nights
- Each night assigned a “wetness scale” severity score:
  - 0 = dry
  - 1 = damp
  - 2 = wet
  - 3 = soaked
- Records if wet during the day
- Records if bowel movement occurred each day
- Any additional relevant comments that need to be mentioned (fluids during the night, illness, sleepover at a friends house, multiple voids during the night, etc)

After 30 days of behavior therapy and recording voiding diaries...

Initiation of TENS therapy

- Day 30 clinic visit
- Randomized into one of 4 arms
- Provided with TENS unit and supplies, taught how to use in clinic with settings provided, and tested for usage ability
- PIN-Q and Month 2 voiding diaries

Treatment Arms

1. Suprapubic TENS
2. Parasacral TENS
3. Posterior tibial nerve TENS
4. Shoulder TENS (control)
TENS therapy

- Performed each night when patient goes to bed
- Treatment session duration\textsuperscript{1,2,3,4}: 15 minutes
  - TENS will stop after 15 min (if set correctly) while patient falls asleep
- Total treatment duration: 30 days
- Settings:
  - Frequency\textsuperscript{1,2,3,4}: 10 Hz
  - Rectangular waveform pulse width\textsuperscript{*}: 0.26 ms
  - Intensity (determined in office): sensitivity threshold of the patient

\textsuperscript{1} Alcantara (2015), \textsuperscript{2} Barroso (2006), \textsuperscript{3} Bouali (2015), \textsuperscript{4} Lordello (2010)

\textsuperscript{*} Expert opinion from physical therapist

Month 2 voiding diary

- Additional items to record:
  - Time spent using TENS on each nightly session (should be 15 min)
  - The frequency setting used (ensure 10 Hz is being used)
  - Any problems or adverse reactions that may have occurred
- Patients will be encouraged to call the clinic with any questions or concerns

After 30 nights of TENS therapy and recording voiding diaries...

Post-TENS follow up

- Day 60 clinic visit
- Examine patient and address any patient concerns
- PIN-Q and Month 3 voiding diaries (same as Month 1)
After 30 days OFF of TENS therapy and still recording voiding diaries...

**Durability Assessment**

- Day 90 clinic visit
- PIN-Q and ask yes/no: “would you use TENS therapy again for your [child’s] bedwetting?”

**Analysis**

- TENS efficacy (TENS vs pre-TENS months) for each group:
  - Reduction in wet nights per month?
  - Reduction in severity of wetness (wet scale) each night?
  - Improvement in QOL (PIN-Q)?
- Compliance rates and adverse reactions with TENS therapy for each group
- Durability assessment (post-TENS vs TENS months)
TENS 3000

- Analog
- Timer included
- Easy to use
- High quality
- Great reviews

Settings

- Mode: B, N, M
- Pulse width (µs): 30-260
- Pulse rate (Hz): 2-150 ...use 10
- Timer (Min): 15, 30, C
- Intensity (dial on top): 1-8 ...to tolerance

Total patients per study

- 32 patients per group gives the study a power of 80% (standard for research)
- 32 patients x 4 arms = 128 patients
Arms

- Suprapubic (Belly/Bladder) TENS
- Parasacral (Back/Butt) TENS
- Posterior tibial (Ankle/Foot) TENS
- Shoulder / Scapula (Control/Sham) TENS

Suprapubic group

- Place TENS electrode pads onto suprapubic region of the lower abdomen
  - 2 finger breadths above pubic symphysis on either side of the midline spaced 2 finger breadths wide apart from each other

Parasacral group

- Place pads bilaterally over S3 foramen: medial to upper edge of greater sciatic notch and one finger breadth from the sacral spine in the midline
- In adults, we measure 9 cm superiorly from the tip of the tailbone and 2 cm lateral
- Just lateral and superior to the very tip of the “buttcrack” on the top of the butt just before it curves up to the straighten to the back

Posterior Tibial group

- Place one pad behind (posterior to) the medial maleolus of the ankle, and the other pad underneath the arch of the foot on the sole
Shoulder group

- Place both pads over the scapula

Pilot Study

Will determine optimal location for TENS to direct future research into optimizing therapeutic management protocols

Potential

- A promising treatment option in a common pediatric problem without current great solutions
- Will save patients from side effects of meds or complications of more invasive procedures
- Patients can perform at home making it more convenient, potentially improving compliance and thus efficacy of treatment
Preliminary Analysis: TENS for PNE

- Over 148 patients recruited into study
  - 58 LIJ, 90+ AMC
  - 100 randomized
  - In analysis: Month 1 – 82, Month 2 – 59, Month 3 – 29
  - No adverse reactions

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<th></th>
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<th>TENS compliance</th>
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<tr>
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<td>Group</td>
<td>Mean age (range)</td>
<td>F/M</td>
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<td>Ankle</td>
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QOL with TENS therapy

![Graph showing PIN-Q score improvement with behavioral modifications over one month of TENS therapy.](image)
Reduction in wet nights with TENS

Severity of wet nights with TENS

Durability of TENS therapy

Final Thoughts

- When combined with behavioral modifications, TENS therapy before bed each night appears to be beneficial for nocturnal enuresis, with posterior tibial TENS showing the best results.

- Our next studies will likely use the posterior tibial location on the ankle to determine optimal pulse frequencies, widths, and modes for use.
References


Thank you!

Any questions?