Noninvasive Electrical Stimulator as an Adjunct for Pain Control After Ureteroscopic Stone Management

Study Protocol and Statistical Analysis Plan

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Study Title:
Treatment of Ureteral Stent Pain with a Transcutaneous Electrical Nerve Stimulator (TENS for US)

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Background:
Ureteral stent placement is one the most common and frequent procedures performed post-uretereoscopy.[5] A double J-stent is the common type of stent used during the ureteral stent placement procedure. The 'pigtail' design of the stent prevents it from migration. Although there is no clinical evidence why stenting is required, but many studies indicate a few reasons why stenting might be required, and this includes ureteral dilation, trauma to ureter due to constant in and out of the ureter during ureteroscopy, leaving behind large stone fragments, impacted stone, misfiring of laser during ureteroscopy etc. [1,2,3] The stent is used to maintain the ureter patency, recovery and/or prevent obstruction due to inflammation caused during the ureteroscopy procedure. The stent is typically removed after 3-7 days, a duration long enough for the ureter to heal itself from the trauma caused by the ureteroscopy procedure.[6]

Despite the benefits of placing a stent post-ureteroscopy, eighty percent of patients with ureteral stents complain of a various side effect from the stent with the most common complaint being lower back pain. This pain is thought to occur through the same mechanism of action i.e., back pressure into the renal pelvis, as an obstructed kidney stone.[4,5] The ureteral stent keeps the ureter open and the urine flows through this stent in both directions i.e., towards the bladder or back to the kidney due to it being an open tube. When the urine flows back to the kidney due to pressure in the bladder, it creates the same back pressure as an obstructing stone in the ureter, and results in similar lower back pain that can be as severe as the pain with an obstructed stone.

To manage the pain and discomfort associated with the ureteral stent, some physicians will prescribe pain medications, such as Tylenol, Motrin, NSAIDs, or Opioids. Patients will fall back to any of these pain management medications, specifically Opioids, when their pain is intolerable. Opioid addiction is an epidemic in US, there are numerous initiatives to curb this crisis starting from limiting the number of opioid prescriptions.

In an effort to find new and alternative ways of treating this pain, we are conducting a study on Transcutaneous Electrical Nerve Stimulation (TENS) to measure its effect on reducing the pain caused by ureteral stents and compare it to the standard of care practice that does include various pain management medications.

In this study, the team is proposing to recruit 60 patients who underwent a kidney stone procedure with a post procedural ureteral stent. Thirty of the sixty patients will be randomized

and discharged with a TENS device (treatment group) that they will use over a course of 3-7 days (typical duration of a stent in the patient) to see how the device helps in treating their pain associated with the stent. The electrode pad will be applied to the lower back near the paravertebral position and the site of pain (Figure 3). The remaining 30 randomized patients will be in the control group, and will not receive a TENS device. All 60 patients are required to complete a daily pain visual analog score (VAS) score along with their daily pain medication intake. Once the stent is removed in the physician's clinic during their follow up visit, they will hand over the TENS and complete a survey of their experience and pain score with the device. These survey results from the treatment group will be compared against the control group to measure efficacy and safety of the TENS device for treating renal colic pain.

The study will not otherwise affect the care a patient will receive. The TENS group will receive the same standard of care treatment as the non-TENS group, but the TENS group are asked to use the TENS device 4 times a day for 60 minutes during each treatment while they have the ureteral stent placed in their body.

Objectives:

1) Primary outcome – To determine the patient with the TENS unit had a lower reported pain and nausea VAS score compared to control (non-TENS) group
2) Secondary outcome – To determine the patient with the TENS unit took less number of opioids during the duration of stent placed in their ureter compared to control (non-TENS) group

Methods and Measures

This will be a randomized control trial with subjects randomized to either the standard of care pain-relief group or an FDA-cleared TENS unit. The TENS group will follow the standard of care pain-relief group if they are intolerance to TENS or they are seeing no benefits from the TENS unit during the duration of the study. If they stop using TENS or continue following the standard of care treatment intervention, they will document such in the daily survey form.

Participants will be enrolled when they are seen in the Urology clinic for their ureteroscopy procedure scheduling. Participants with kidney stones who are consented for a ureteroscopy will be eligible for the study. Participants will be informed during the enrollment and consent process that if they decide to participate in the study, they will be randomized to receive a TENS unit or the typical standard of care treatment. They can elect to decline the enrollment based on that information, or if they choose to enroll, then they will sign the consent form for participating in the study.

Randomization participants using random generator will be performed by the urology physicians or residents in the preop area of the 300 Pasteur Drive hospital. The patient will be notified in the preop are which study group they are being assigned to, and they will be given further instructions and training post-ureteroscopy procedure in the PACU area. TENS group will be discharged with a TENS unit along with training and instructions on how to use the device. All participants will be instructed to complete a daily survey at the end of day and a final

survey at the time of stent removal. All follow up care will be performed remotely. Participants enrolled in the TENS group will return their TENS unit during the stent removal in the physician's office.

The device settings will be adjusted beforehand and will be the same for every participant, unless it is felt to be too strong, in which case a lower intensity (current intensity with no changes to other stimulation parameters) setting will be used. It should cause no more than minimal tingling to the area on the back where it is applied. The placement of electrode pads will be determined in the PACU area post-ureteroscopy, and the participants will be trained to the device settings and electrode pad placement.

Participant Selection Criteria:
Inclusion

- Adult patients undergoing standard of care ureteroscopy and laser lithotripsy for urinary stone disease
- Patients receiving a stent following their ureteroscopy and laser lithotripsy

Exclusion

- Children
- Pregnant patients
- Patients unable to answer pain questionnaire
- Patients undergoing PCNL
- Patients being treated for Urologic malignancy with ureteroscopy
- Patients who require long term or chronic ureteral stent management
- Patient with implantable stimulators
- Patient with epilepsy
- Patients undergoing laser lithotripsy without stent placement

Sample Size
60 participants with 30 participants in each group

Outcome Measures:
Primary outcome will be to measure and compare daily pain score on a VAS 11-point scale in the TENS group vs control group. Secondary outcome will be the amount of pain medication used in TENS group vs the control group.

Statistical Plan:
The two groups will be analyzed using t-tests or ANOVA, and the final results will be analyzed using descriptive analytics. A regression analysis will be performed for independent outcome prediction.

Recruitment Methods and Consent
All participants will be recruited during their outpatient consultation for kidney stones with the urology clinic. Participants who are scheduled for a standard ureteroscopy procedure with laser

are eligible for the study and they will be informed about the study. The consent form will be shared by the attending physician to the participant during their initial consultation visit and the participants will have sufficient time to make a decision if they want to participate or not. Signed informed consent form will be obtained for each participant before their ureteroscopy procedure.

Reporting of Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

References:

1. Tang et al., “Placement of Ureteral Stent After Uncomplicated Ureteroscopy.”
2. Byrne et al., “Routine Ureteral Stenting Is Not Necessary after Ureteroscopy and Ureteropyeloscopy.”
3. Foreman, Plagakis, and Fuller, “Should We Routinely Stent after Ureteropyeloscopy?”
4. Koprowski et al., “Ureteral Stent-Associated Pain.”
5. Miyaoka and Monga, “Ureteral Stent Discomfort.”
6. Sali, Gaurav Mohan, and Hrishikesh B. Joshi. “Ureteric Stents: Overview of Current Clinical Applications and Economic Implications.”