

# **Preoperative Antibiotics for Carpal Tunnel Release Surgery**

NCT 03432858

*Endoscopic Carpal Tunnel Release, Infection Incidence, and Prophylactic Antibiotics: Indicated or kick the habit?*

**Document Date: October 10, 2018**

# **Title: Endoscopic Carpal Tunnel Release, Infection Incidence, and Prophylactic Antibiotics: Indicated or Kick the Habit?**

**Version: 1.6**

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## Protocol

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### **A. Background**

Each year, one million adults in the U.S.A are diagnosed with carpal tunnel syndrome (CTS) with 500,000 carpal tunnel release (CTR) procedures. Previous analyses have shown very low rates of surgical site infections (SSI) overall<sup>2,10</sup> with incidence rates of 0.25-0.77% without or 0.21-0.47% with surgical prophylactic antibiotics, but no statistical significance.<sup>1,2,9</sup> These include populations typically considered “high risk” such as those with diabetes mellitus, or history of total joint arthroplasty.<sup>2,3</sup> Despite both American and international current literature demonstrating low incidence of

infection in all types of CTR, and recommendations to discontinue habitual use of preoperative antibiotics in clean hand surgery, the behavior is still very prevalent with 30-60% of hand surgeons still prescribing either sometimes or all the time prior to CTR.<sup>2,7,9,11,12</sup> Only 2% of British hand surgeons prescribe prophylactic antibiotics before CTR. In Canada CTR surgery is considered minor, even being performed routinely in the clinical office setting, and all without prescribing antibiotics prophylactically.<sup>5</sup> Endoscopic carpal tunnel release (ECTR) procedures are becoming more common, and while current evidence supports no significant increased rates of complications, without direct visualization and hemostasis there is potential for hematoma vulnerable to infection. While there is some appropriately powered,<sup>12</sup> prospective<sup>8,12</sup> level I evidence regarding the use of prophylactic preoperative antibiotics in carpal tunnel surgery in general, to our knowledge there are none specifically investigating incidence of SSI with and without antibiotics after ECTR.

## **B. Objective(s)**

Establish level I evidence regarding

- whether prophylactic antibiotics reduce the incidence of infection in ECTR

## **C. Study design**

- Procedures by fellowship-trained hand surgeons.
- Prospective, randomized, and double blinded.
  - **RANDOMIZATION:** Participants will be randomly assigned to 1 of 2 groups: 1) Weight-based Ancef (or 1 g of vancomycin if penicillin/cephalosporin allergic) within 30 minutes of incision; or 2) placebo IV of normal saline.
  - **BLINDING:** Neither surgeon, nor investigators, nor patient will know who did or did not receive antibiotics until the end of the project. Randomization generator will be utilized by Emig Research Center associate to create a master copy, with subsequent sealed copies maintained at Emig Research Center, with Orthopaedic Residency Research Coordinator (Chelsea), and the WSRH pharmacy.

The patient number (P#) list will be held by the preoperative surgical scheduler, who will not participate in data collection nor follow-up.

The corresponding decoder key of P# with associated randomized number will be held by WSRH Pharmacy for collaboration to formulate the indicated antibiotic or placebo solutions preoperatively.

- **PRIMARY OUTCOMES:** Determine proportion of patients with SSI in antibiotic versus placebo group. Subjects follow-up over six weeks with primary outcomes being (1) “any supplemental intervention” (i.e. additional wound care, antibiotics, or revision surgery.); and (2) declaration of “complete” healing by six weeks post-operative.
  - 2 weeks - clinical wound check.
  - 6 weeks – clinical assessment for completion of wound healing.
  - At each visit the attending physician will designate as “infected” or “not infected” and will be allowed to treat each patient accordingly. Designations will be based on either:
    - Clinician experience
      - Considerations include but are not limited to painful incision, erythema, drainage, or wound dehiscence.
    - Culture confirmed
      - deep infections
  - Wounds designated “infected” by the treating surgeon will be sub-divided into:
    - Superficial (Surface only)
      - Treatment with local wound care
      - Oral antibiotics only
    - Deep
      - IV antibiotics only
      - Surgical Irrigation & Debridement and IV antibiotics.
- **SECONDARY OUTCOMES:**
  - Demographic information as well as comorbidities such as: acuity of CTS, time from last cortisone injection, diabetes<sup>2</sup>, smokers, COPD, anemia, peripheral artery disease, history of arthroplasty<sup>3</sup>, valvular disease, and

dual or single incision ECTR will be noted for secondary outcome correlations.

- **DURATION:** By current estimates of 10 CTRs per week, this would require 65 weeks, with another 6 weeks to complete observations of the patients.
- **PROCEDURE:** Dual or single-incision endoscopic carpal tunnel release with steri-strip closure and simple sterile dressing, without immobilization.
- **WOUND CARE & ACTIVITY:** Non-weight bearing on affected extremity until 2 week follow-up appointment. May shower post-operative day 4, but no submersion. 5 lb. weight restriction for 2 weeks, then 10 lbs for 3 weeks. No physical therapy.

## **D. Study population and recruitment methods**

- From the investigator's private clinical practices, all those who meet criteria for carpal tunnel release will be offered to participate in the study.

## **E. Inclusion and exclusion criteria**

- **INCLUSIONS:** All patients who meet high probability (>12 points) on the Carpal Tunnel-6 (CTS-6) diagnostic aide and recommendation for carpal tunnel release who are capable of giving informed consent, or their legal representative on the patients behalf.
- **EXCLUSIONS:** Patients allergic to both penicillin/cephalosporins and vancomycin. Patients immobilized with splint or cast or receiving formal physical therapy in initial 6 weeks after ECTR. Children under the age of 18 years old. Patients or their legal representatives who decline the invitation for participation.
- **VULNERABLE POPULATIONS:** Pregnant females and prisoners will be treated with equal and safe fairness and randomization as other participants, both pre-procedure as well as post-procedure, due to the double-blinded nature of the antibiotic administration. They will stand to benefit from the investigators clinical suspicions for infection without potential conflict of interest with study outcomes.

## F. Role of subjects

- Participants will agree to follow-up at 2 and 6 weeks in the clinic, as is already standard of care.
- Participants will be asked to notify providers if concern for or signs of infection arise.

## G. Research procedures

- Patient identified with score  $> 12$  (80% probability) on the CTS-6 and recommended CTR: (<http://www.orthoguidelines.org/ctsdagnosis>)<sup>6</sup>
  - Symptoms predominantly in medial nerve innervated digits
  - Nocturnal numbness
  - Thenar atrophy and/or weakness
  - Positive phalen test
  - Positive tinel sign
  - Loss of 2-point discrimination
- Surgeon will discuss risks, benefits, and alternatives to surgical intervention.
- Patients who elect to proceed to scheduling will be invited to participate in the study and informed consent will be obtained prior to seeing surgical scheduler.
  - For those who decline participation, they will be directed to scheduling without tardiness or punishment.
- After scheduling surgery, the surgical coordinator will place a patient study number (P# ie. P1, P2, P3, P4...) sticker on the patients surgical consent and participation consent and these will be scanned into the Epic Electronic Medical Record (EMR) under “Media – Study: ECTR”

Patient will be “tagged” with a study tag on their record banner for 6 weeks.

Patient will be added to “ECTR & ABX” custom patient list.
- A “miscellaneous order” to pharmacy will be placed in the Day of Surgery orders indicating need to blind the antibiotic solution as well as the P#.
- Pharmacists at WellSpan Surgical & Rehabilitation Hospital will possess a copy correlating randomization numbers to each P# with instruction to formulate a placebo bag of normal Saline for all ODD numbers, or an infusion of **IV antibiotics** (Ancef or Vancomycin for

PCN or Cephalosporin allergic) for all EVEN numbers on the day of surgery.

*-Example-*

*Patients p1,p4, and p5 (Even) receive antibiotic.*

*Patients p2, and p3 (Odd) receive placebo.*

1 Set of 650 Unique Numbers

Range: From 1 to 650

Set #1

p1=110, p2=333, p3=107, p4=570, p5=62, p6=318, p7=22, p8=626, p9=259,  
p10=471, p11=92, p12=477, p13=194, p14=218, p15=190, p16=443, p17=394,  
p18=47, p19=327, p20=37, p21=595, p22=598, p23=308, p24=264, p25=12,  
p26=428, p27=201, p28=228, p29=121, p30=255, p31=212, p32=184,  
p33=144, p34=419, p35=583, p36=328, p37=597, p38=285, p39=539, p40=46,  
p41=131, p42=166, p43=610, p44=608, p45=390, p46=335, p47=84, p48=302,  
p49=211, p50=518, p51=311, p52=629, p53=89, p54=383, p55=430, p56=503,  
p57=267, p58=398, p59=113, p60=454, p61=550, p62=468, p63=416,  
p64=338, p65=98, p66=450, p67=193, p68=317, p69=444, p70=588, p71=148,  
p72=475, p73=1, p74=291, p75=408, p76=213, p77=546, p78=460, p79=612,  
p80=207, p81=75, p82=357, p83=34, p84=26, p85=489, p86=488, p87=13.

- On the day of surgery, blinding will continue with appropriately patient labeled IV bag without identifying markers of content, to be administered within 30 minutes of surgical incision.
- Surgical prep will be with chlorhexidine gluconate scrub and standard sterile draping and technique.
- Patients will undergo routine procedure with dual-or-single incision, single nylon closure, and simple adhesive steri-strip cover, without immobilization.
- Wound will be visually evaluated at 2 & 6 week follow-up appointments
  - Activity limitations will include:
    - 5 lbs maximum for first two weeks
    - 10 lbs maximum for for two to six weeks
    - followed by “no restrictions” at 6 week appointment.
- After the 6 week appointment of every 25<sup>th</sup> patient, investigators may “break the seal” and insert patient information from the prior 25 patients into protected collection data tables for final evaluation at study completion.

## H. Data to be utilized

- Demographic information
- Medical comorbidities and history from clinic notes and Epic EMR.
- Excel Spreadsheet with de-identified data collection

## **I. Data analysis**

- **POWER:** Statistical significance would require n= 92 split evenly between trial and control; but clinical significance requires greater numbers due to the low incidence (0.25%-1.5% in the retrospective literature.)<sup>8,9</sup>
  - Our goal was calculated using the median incidence of 0.40%,<sup>5</sup> for a calculated power of **n=642** split evenly between trial and control.
- **STATISTICAL ANALYSES:**
  - Data will be analyzed using the statistical analysis program, SPSS. Most analysis will be completed by scientific support staff of the EMIG Research Center. Analysis will include frequency and percent determinations for all categorical parameters and mean and standard deviations for all continuous parameters. Appropriate statistical tests will be employed to determine any statistical differences or associations between groups or subgroups once they are identified, which may involve chi-square, ANOVA, regression, or independent sample t-testing.

## **J. Risks and risk management**

- Patients will not be pressured into participation.
- Grant funding will cover the cost of study drug to which patients are assigned. Patients and/or patient insurance will not be responsible for the cost of the study drug. more than the current intermittent costs of occasional antibiotic use.
- Insurances will be billed as usual for all other ESCR surgical costs.
- Self-pay patients will be treated equally with insured patients.
- The risk of disruption to patient life, work, or social risk are low since this protocol allows for appropriate intervention at all points along the patients 6 week course.
- An interim data analysis will occur beginning at patient number 25 to ensure that study procedures are not causing harm. The data analysis will be conducted by the research associate. The co-investigator will review the results, and the PI will determine if it is safe to continue the study.

## **K. Benefits**

- Study patients are not expected to directly benefit from participation.



- Patient and societal benefits will be related to surgeons doing our part to appropriately manage antibiotic stewardships, and decrease risks of antibiotic-resistant organisms.
- Professional benefits would include support for decisions to eliminate unnecessary antibiotic prophylaxis in clean hand surgery; OR establish the risks and utility of ECTR and antibiotics compared to traditional surgery and preoperative protocols.
- Economic implications include:
  - 500,000 procedures yearly with around 165,000 receiving antibiotics preoperatively, at estimated \$50/2grams Cephazolin (or \$150/1g Vancomycin), could save \$8,745,000 yearly nationally (est. with Cephazolin).
  - Antibiotics are expected within 30 minutes of incision, and will occasionally delay incision in the operating room while the antibiotic is administered. Estimated costs for OR function range from \$20-60 per minute. Thus even a 3 minute delay for rapid IV infusion, during a 15 minute procedure, wastes another \$60-180 per procedure.
  - Up to \$330 extra cost per procedure for administration of a potentially unnecessary treatment.

#### **L. Compensation / incentives and research-related costs**

- Compensations/Incentives: None
- Costs: Grant funding has been secured through Lake Erie College of Osteopathic Medicine (LECOM) to cover the cost of IV saline and antibiotics to avoid additional costs to the patient. Research time and product will be supplied by the primary and co-investigators and the Orthopaedic Surgery Residency research fund.

#### **M. Alternative procedures**

- Potential subjects are not required to participate in the study and refusing to do so will not affect the quality of their treatment.

#### **N. Research materials, records, and confidentiality**

- All patient records will be obtained through the secure WellSpan Health EMR (Epic).

- Information will be stored external to the system in a non-identifiable manner with a P# assigned to individuals on password encrypted hospital and private computers in an Excel spreadsheet.
- No patient information will be accessed outside of typical patient care unless a signed HIPAA authorization form for participation in the study is in the patient record.

### **O. Subject informed consent**

- **CONSENT:** According to both Federal and State of Pennsylvania law, the surgeon of record will be authorized and trained to provide and obtain informed consent in writing at the preoperative visit.

### **P. Intended use of research**

- Submission of abstracts to national conferences for posters and journals for manuscripts
- Submission to Residents' Research Day

### **Q. Delineation of resources required to conduct the study**

- Emig Research center
- Orthopaedic Residency research coordinator
- Statisticians
- Fellowship-trained Hand Surgeons
- Hand Surgery Fellow(s)
- Orthopaedic Residency resident of Hand service
- Pharmacists
- Pharmacy technicians
- Anesthesiologists
- Numerical Randomization generator
- SPSS statistical software
- Microsoft Office: Word, Excel, PowerPoint

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