

Journal Club / Research Article Summary - (Adapted from Schultz Table)

Date: December 15, 2010

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**ARTICLE:**

- *Citation:* Randomized, Double-Blind, Placebo-Controlled Trial of Cephalexin for Treatment of Uncomplicated Skin Abscesses in a Population at Risk for Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infection. Rajendran PM et al. *Antimicrobial Agents and Chemotherapy*. Nov 2007; 51(11):4044-4048
- *Country:* USA
- *Funding Sources:* NIH-Division of Research Resources, USPHS, UCSF Dean's Fund for Research, Doris Duke Charitable Foundation

**PURPOSE:**

- *Research Question(s):*
  - (i) to compare a current "standard of care" antibiotic, cephalexin, to placebo after surgical incision and drainage of uncomplicated skin abscesses
  - (ii) to establish the prevalence of MRSA in the population under study
  - (iii) to prospectively determine whether discordance between therapy and isolate susceptibility affected outcome
- *Hypothesis:* Empirical use of beta-lactam antibiotics, the preferred agents for treating uncomplicated skin and soft tissue infections, may no longer be appropriate for these infections because of the increasing prevalence of community strains of MRSA

**DESIGN:**

- *Study Design:* Randomized, Double-Blind, Placebo-Controlled Trial
- *Dependent / outcome Variable(s):* Clinical cure or failure 7 days after incision and drainage of skin and soft tissue abscess
- *Independent / research Variable:* Cephalexin 500mg QID x 7 days vs. placebo

**SETTING / SUBJECTS:**

- *Research Setting:* SF General Hospital (urban, academic), daytime-only walk-in outpatient surgery clinic from November 2004 to March 2005
- *Subjects:*

- *Study population:* Outpatient surgery clinic patients at SF General Hospital (population known for high rates of illicit drug injection use; homelessness; infection with hepatitis C, hepatitis B or HIV)
- *Inclusion criteria:*
  - >18y
  - Abscess that attending surgeon believed required surgical intervention and was severe enough that a duration of 5 or more days of antibiotic therapy was anticipated (must meet 2 or more of the following criteria):
    - Acute onset within 7 days of enrollment
    - Purulent drainage or purulent aspirate
    - Erythema, induration (>2cm dia), or tenderness
    - Evidence of loculated fluid at time of enrollment
- *Exclusion criteria:*
  - Unlikely to survive through treatment period
  - Evidence of toxic-shock syndrome or toxic-shock-like syndrome
  - Shock or hypotension, oliguria not responsive to fluid challenge
  - Incisional wound extending into visceral compartments
  - Suspected or proven contiguous joint or bone involvement
  - Ischemic ulcers or wounds associated with arterial insufficiency or gangrene
  - Infection of prosthetic materials or venous catheters that could not be removed as part of the treatment for the current infection
  - Infection of a full-thickness burn wound, or burn wound that was >20% TBSA
  - PCN or cefalexin allergic
  - Renal compromise requiring adjusted dose of cephalexin
- *Number (control / intervention groups):*
  - 713 patients seen in clinic during study period
  - 187 eligible for study (21 refused participation)
  - 166 randomized
    - 82 assigned to receive cephalexin
    - 84 assigned to receive placebo
- *Demographics:* Mostly male, median age 43-45, predominantly Caucasian and African-american, >1/3 homeless (see *Study population* above).
- *Attrition:* 4 total enrollees (2 from each group) were lost to follow-up

## **METHODS:**

- *Interventions:* All enrollees underwent I+D of abscess by an attending surgeon, culture samples collected, wick placed or wound packed after drainage for healing

- by secondary intention, daily follow-up in clinic for wound check and bandage changes, and day-7 follow-up evaluation to evaluate for clinical outcome.
- *Study Groups:* Study group received Cephalexin 500mg PO QID x 7 days, Control Group received placebo PO QID x 7 days.
  - *Instruments:*
  - *Data Collection:* Data was collected by attending surgeon and nurse practitioners in the surgical clinic.

#### **DATA ANALYSIS:**

- *Level of Data/Statistics Used:* Dichotomous variables were analyzed using Fisher's exact test. Ordinal variables were analyzed using the Kruskal-Wallis test. Continuous variables were analyzed with Mann-Whitney tests.
- *What, if any, variables were controlled for?:* Patients who did not return for follow up, who could not be contacted by phone, and whose outcome could not be determined from chart review were deemed failures.

#### **RESULTS:**

- *Brief answers to research questions:*
  - (i) to compare a current "standard of care" antibiotic, cephalexin, to placebo after surgical incision and drainage of uncomplicated skin abscesses
    - Cephalexin (84% cure rate)
    - Placebo (90% cure rate)
  - (ii) to establish the prevalence of MRSA in the population under study
    - 50% prevalence
  - (iii) to prospectively determine whether discordance between therapy and isolate susceptibility affected outcome
    - No effect on outcome
  - This study indicates that cephalexin does not have a significant benefit in addition to incision and drainage for uncomplicated skin abscesses.
- *Additional findings:*
  - Subgroup analysis of demographics, co-morbidities, abscess characteristics – data not powered to find significant differences between groups, though data suggests that these groups would not change overall trend in results/outcomes
- *Limitations:*
  - No active treatment arm (beta lactams have no useful antimicrobial effect on MRSA). Though the study does cite observational retrospective studies showing no difference in outcomes when beta lactams are compared to antibiotics to which MRSA is susceptible.
  - Recurrence rates not determined, therefore true "cure rates" may be misleading.

- Single site outpatient clinic setting not necessarily representative of general populations (not to mention the fact that 48% of enrollees were known IV drug users).
- Procedures performed by attending surgeons
- Only 1 of 166 enrollees were febrile – may not be generalizable to all populations

**IMPLICATIONS FOR PRACTICE:**

- *Applicable to this clinical practice:* The study population shares some similarities to our patient population, however not directly generalizable to ED patients in Portland Maine.
- *Feasible (cost, resources, etc):* I+D instruments are inexpensive, expertise is readily available in the ED. Antibiotic administration after I+D in the ED is a relatively low cost (and routine) practice for some providers.
- *Clinically Relevant:* Yes

**LEVEL OF EVIDENCE / DECISION FOR USE:**

- Background  Consider Replication  Ready for use
- *Level of Evidence:*
  - Ia Evidence obtained from meta-analysis of randomized controlled trials
  - Ib Evidence obtained from at least one RCT
  - IIa Evidence obtained from at least one well-designed controlled study without randomization
  - IIb Evidence obtained from at least one other type of well-designed quasi-experimental study
  - III Well-designed non-experimental studies
  - IV Expert committee reports, opinions of experts