Official Title: Antibiotic Irrigations for Intra-Abdominal Drains

NCT Number: NCT03476941

Document Date: May 18, 2020

Project Title: Antibiotics Irrigation for Intra-Abdominal Drains

Principle Investigator: Scott Sherman, MD

Purpose:

Intra-abdominal abscesses are pus-filled pouches in the abdominal cavity. Current standard of care includes drain placement in the abscess cavity to reach source control as well as administration of systemic antibiotics. The drain is flushed with normal saline on a daily basis to ensure patency. This study aims to analyze the clinical impact of a higher local concentration of antibiotics (rather than normal saline) provided through drain irrigation with an antimicrobial agent (Gentamicin).

Study aims or hypotheses:

Goal of this study is to evaluate the clinical efficacy of direct abscess antibiotic irrigation through an abdominal catheter. Hypotheses:

- Improved clinical course: white blood count rate, temperature curve, time on vasopressors
- Shorter length of systemic antibiotic therapy and indwelling catheter
- Lower incidence of side effects attributable to systemic antibiotic therapy (including Clostridium difficile infections)

Background and significance:

There are data to support antibiotic containing peritoneal lavage in colorectal surgery can decreased the intra-abdominal abscess (Ruiz-Tovar et al 2012). This study has used clindamycin-gentamicin solution for peritoneal lavage in this prospective, randomized study of 103 patients. The study has demonstrated that presence of antibiotics in peritoneal wash plays additional role to dilution and mechanical clearance of the bacterial loads in preventing intra-abdominal abscess. The antibiotics irrigation of various drain and catheters has been performed with good results in the setting of ventricular drain and urinary catheters. Intraventricular administration of gentamicin has been shown to effectively treat ventriculitis. However, to date, there is a lack of data on the effect of direct antibiotic irrigation of intra-abdominal abscesses. Based on the previously mentioned study, clindamycin and gentamicin were selected for our study.

Procedures:

Patients will be consented to receive antibiotic irrigation's through their drain. No additional action is required on their end. It is important to note that currently patients receive saline irrigation of their drain. This means that our study does not actually require additional time/action burden on the patient.

- The procedures will occur for up to seven days while patient are admitted.

- The procedures may be terminated earlier than seven days if decision is made to remove the drain within 7 days of placement.

- There is no need time commitment for the subject.

- Clinical outcomes may be collected up to 30 days post discharge.

- Subject participation in the study will last approximately 30 days with no additional follow up visits as part of the involvement in this study.

- Data from clinical visits and/or follow up within the 30 days will be collected as part of the research.

Target Enrollment and study duration: We are planning on enrolling 50 patients and randomized them to either drain irrigation with saline or gentamicin. The enrollment will continue for 1 year.

Age of Subjects: 18-80 years

Inclusion Criteria:

18-80 years patients; intra-abdominal abscess drained with catheter/drain; systemic antibiotics(piperacillin/tazobactam or ciprofloxacin/metronidazole), ability to understand and comply with the requirements of the entire study and to communicate with the study team.

Exclusion criteria

- Abscess or multiple abscesses not amendable to image guided drain placement.
- Less than 18 years of age.

Arms and Interventions:

Arms	Assigned Interventions
Experimental: Antibiotic Irrigation The drain will be irrigated twice/day with the above antibiotic solution for 7 days maximum	Drug: Gentamicin Sulfate Inj 20mg/2ml vial for injection Irrigate surgical drain with total amount of 5 mg in 10 ml volume twice/day for 7 days or until drain removal if less than 7 days of therapy. Drug: Clindamycin phosphate 6 mg/1ml for injection Irrigate surgical drain with total amount of 12 mg in 10 ml volume once daily for 7 days or until drain removal if less than 7 days of therapy.
Placebo Comparator: Normal Saline Irrigation The drain will be irrigated twice/day with normal saline	Placebo The placebo group will receive drain irrigation twice/day

Outcome Measure:

Primary Outcome Measure:

1) Duration of Systemic Antibiotics: [Time Frame: From initiation of systemic treatment until 1 month follow up]

Secondary Outcome measures:

1) White Blood Count [Time Frame: From initiation of systemic treatment until 1 month follow up]
2) Change in Temperature [Time Frame: From initiation of systemic treatment until 1 month follow up]
3) Changes in Size of the Abscess [Time Frame: From patient initial hospitalization up to 1 month follow up]
4) Changes in Drain Output [Time Frame: From the drain placement up to 1 month follow up]

Risks associated with antibiotics:

Gentamicin risks

• Neurologic: Neuromuscular blockade finding (Temporary or Permanent Weakness)

• Otic: Ototoxicity (Damage to your ear, may affect hearing)

• Renal: Nephrotoxicity (Damage to your kidney, can rarely cause temporary or chronic kidney injury)

• Respiratory: Respiratory tract paralysis (temporary hoarseness, shortness of breath), Concomitant anesthesia, muscle relaxants

Clindamycin risks:

• Dermatologic: Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis (Painful rashes, blisters)

• Gastrointestinal: Clostridium difficile colitis, Hemorrhagic diarrhea, Pseudomembranous enterocolitis (Diarrhea due to infection)

• Hematologic: Agranulocytosis (decrease number of blood cells)

• Hepatic: Increased liver function test (mild injury to your liver), Jaundice (yellowing of the skin)

• Immunologic: Drug reaction with eosinophilia and systemic symptoms (fever, allergic reaction)

Risk of increase antibiotic resistant microorganism:

• Potential risk of increase resistance of bacteria to antibiotic.

Statistical Analysis Plan:

The subjects will be randomized through investigational pharmacy. In general, continuous variables will be summarized using descriptive statistics including the number of observations, mean, standard deviation, minimum, median, and maximum values. Categorical values will be summarized using number of observations and percentages. All statistical tests will be performed at the two-sided, 5% significance level, unless otherwise specified.

This study will collect data for 1 year. Based on previous experience, between 30 and 50 patients undergo drain placement for intra-abdominal infectious processes. Primary end point will be the reduction of duration of systemic antibiotics. Assuming dichotomous outcome (yes/no), and sample size calculation in two independent study group to show 50% of study population to show decrease in systemic antibiotics administration with alpha = 0.05 for type I error and power of 95%, total sample size needed is 32.

References:

- Yoon, Y. I., et al. (2015). "Therapeutic effect of trans-drain administration of antibiotics in patients showing intractable pancreatic leak-associated pus drainage after pancreaticoduodenectomy." Korean J Hepatobiliary Pancreat Surg 19(1): 17-24.

- Sauermann, R., et al. (2012). "Good penetration of moxifloxacin into human abscesses." Pharmacology 90(3-4): 146-150.

- Sauermann, R., et al. (2012). "Abscess penetration of cefpirome: concentrations and simulated pharmacokinetic profiles in pus." Eur J Clin Pharmacol 68(10): 1419-1423.

- Zimmerman, L. H., et al. (2011). "Impact of evaluating antibiotic concentrations in abdominal abscesses percutaneously drained." Am J Surg 201(3): 348-352; discussion 352.

- Rink, A. D., et al. (2008). "Pharmacokinetics and tissue penetration of moxifloxacin in intervention therapy for intra-abdominal abscess." Clin Drug Investig 28(2): 71-79.

- Wagner, C., et al. (2006). "Principles of antibiotic penetration into abscess fluid." Pharmacology 78(1): 1-10.

- Sauermann, R., et al. (2005). "Antibiotic abscess penetration: fosfomycin levels measured in pus and simulated concentration-time profiles." Antimicrob Agents Chemother 49(11): 4448-4454.

- Leborgne, F. and F. Leborgne (2003). "Treatment of breast abscesses with sonographically guided aspiration, irrigation, and instillation of antibiotics." AJR Am J Roentgenol 181(4): 1089-1091.

- Joukhadar, C., et al. (2003). "Target site penetration of fosfomycin in critically ill patients." J Antimicrob Chemother 51(5): 1247-1252.

- Akimoto, Y., et al. (1996). "Cefaclor concentration in pus from abscess caused by odontogenic infection after a single oral administration." Gen Pharmacol 27(1): 177-179.

- Akimoto, Y., et al. (1994). "Amoxicillin concentration in pus from abscess caused by odontogenic infection." Gen Pharmacol 25(1): 111-113.

- Terada Y, Mineharu Y, Arakawa Y, Funaki T, Tanji M, Miyamoto S. "Effectiveness of neuroendoscopic ventricular irrigation for ventriculitis." Clin Neurol Neurosurg. 2016 Jul;146:147-51.

- Hill DM, Wood GC, Hickerson WL. Linezolid bladder irrigation as adjunctive treatment for a vancomycin-resistant Enterococcus faecium catheter-associated urinary tract infection. Ann Pharmacother. 2015 Feb;49(2):250-3.