Prospective study investigating antibiotic elution from free intra-articular vancomycin and tobramycin powder after cementless total knee arthroplasty

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OVERVIEW

Background information:
Use of intrawound antibiotics to decrease the risk of periprosthetic joint infections (PJI) is standard practice in primary total knee arthroplasty (TKA). There is mixed evidence on their role in reducing infection rates after TKA. For cementless TKAs, surgeons typically add an antibiotic to the knee prior to closure. Previous studies have showed that the systemic absorption of these antibiotics is low, and they carry a low risk of toxicity.

Prior studies have shown that many of organisms causing PJI after primary TKA are susceptible to vancomycin but resistant to aminoglycosides including tobramycin. These findings have been confirmed by our previous study on bacterial isolate patterns from PJIs after TKA. It showed that nearly all of the gram negative isolates were susceptible to tobramycin, while 27.8% of the gram-positive isolates were resistant. However, the addition of vancomycin covered 100% of these tobramycin-resistant gram-positive isolates. Thus, the addition of vancomycin and an aminoglycoside together provides broad-spectrum prophylaxis against the most common organisms causing PJIs after TKA.

Primary Hypothesis:
The intra-articular concentration of vancomycin and tobramycin will reach supratherapeutic concentrations postoperatively. Serum concentrations will be significantly lower than intraarticular concentrations. Use of these antibiotics is an effective way to reduce joint infections.

Aim(s):

1. Determine the intra-articular concentration of vancomycin and tobramycin after administration of vancomycin and tobramycin powder in primary cementless total knee arthroplasty.
2. Determine the serum concentrations of these antibiotics postoperatively

Potential Contribution:
The findings of this study will provide evidence for optimal intrawound antibiotic choice in cementless total knee arthroplasty.

METHODS
Timeline: 1 year (6 months of prospective enrollment and 6 months of data analysis.)

Data analysis will begin after this study has received approval. Anticipated end date is December 2020.

Inclusion/Exclusion Criteria:

1. Age over 18
2. Total knee arthroplasty for primary osteoarthritis Primary diagnosis of knee osteoarthritis

Exclusion criteria:
1. Diminished mental capacity
2. Vancomycin allergy
3. Tobramycin allergy
4. Chronic kidney disease stage III and stage IV

Recruitment:
We will be identifying patients from the clinical practice of Dr. Ryan Nunley, Dr. Robert Barrack, and Dr. Charles Lawrie.

Design:
This study is a prospective study designed to characterize and quantify the level of antibiotics eluted from the knee after administration of intrawound antibiotic powder in primary cementless total knee arthroplasty.

The study will collect 3 samples of postoperative intra-articular drain fluid from the total knee arthroplasty, and 3 samples postoperative serum samples the day after surgery. The total amount of intra-articular drain fluid and blood drawn will be 15 mLs fluid and 15 mLs blood, respectively. (5mL = 1 teaspoonful 15mL=1 tablespoonful) The fluid being used for the study is fluid that is drained after surgery and discarded. Data collected will permit clinical evaluation of antibiotic powder as it pertains to total knee arthroplasty. This study will collect drug-related or possibly drug-related adverse events. Data collected will include the following: Patient demographics (age, gender, BMI), implant and surgical information, and medical comorbidities. Each eligible participant will be required to execute written informed consent and covers the provisions of this study.

Number of participants: We propose to enroll 20 participants undergoing primary cementless total knee arthroplasty.

There will only be one study group.

The study patients will not be blinded to their study group. The surgeons and study personnel will not be blinded to study group.

Data collection:

Data collection for prospective patients will occur preoperatively and postoperatively.

Data analysis:
A student t-test will be used to compare means and standard deviations between serum and intraarticular antibiotic concentrations. Descriptive statistics will be used to analyze the subjective data points such as AEs. Analysis methods will be further discussed during data and publication review meetings. We will be doing the analysis at pre-operative, intraoperative and postoperative time points. An independent statistician, independent of the study team and the orthopedics department will analyze the data.

Procedures:
The study will collect intraarticular drain fluid from the total knee arthroplasty the day after surgery. 2 serum samples will also be collected after surgery, and there will be a chart review.

INFORMED CONSENT
Enrollment and consent will begin in the clinic of Dr. Ryan Nunley, Dr. Robert Barrack, and Dr. Charles Lawrie. The treating surgeon will identify patients who are determined to be candidates for primary TKA, and who generally meet the study requirements.

The consent process will occur by one of the following means:

1) The study coordinator will meet with each potentially eligible participant to review the study requirements (including additional screening for eligibility) and answer any questions the patient may have.

If the patient has any clinical questions that cannot be answered by the study coordinator they will be answered by the physician or the physician's nurse. The patient will have the opportunity to review the consent form, discuss with family/friends, and do his/her own research on the subject if desired. Qualified patients who agree to participate in the study will be required to sign an Informed Consent Document. Valid enrollment is not granted until after surgery, once it has been verified that the participant has had total knee surgery.

2) The consent discussion and review of the Informed Consent Document may occur over the phone. In this case, the study coordinator will call the patient to present the study to the participant and gauge interest in participation. If the patient expresses interest in participation, the study coordinator will e-mail, mail or fax the Informed Consent Document to the participant. The patient will be given the opportunity to ask questions. If the patient has any research questions beyond the scope of the study coordinator, arrangements will be made for the participant to speak with the applicable member of the research team, including the PI. After review of the Informed Consent Document, the participant will sign the applicable sections of the Informed Consent Document and mail or fax the consent for back to the study coordinator. The Informed Consent Document will be signed by the consenting study coordinator upon receipt. Valid enrollment is not granted until after surgery, once it has been verified that the participant applicable member of the research team, including the PI. After review of the Informed Consent Document, the participant will sign the applicable sections of the Informed Consent Document and email, mail or fax the consent for back to the study coordinator.

PROCEDURES FOR MAINTAINING CONFIDENTIALITY

Data Security:

Protection of confidentiality by the Washington University Coordinating Center will be maximized by use of (a) protected and secured data collection, (b) password protected access to data storage, and (c) access to patient data limited to the study coordinator or his designate.

ASSESSMENT OF RISKS AND BENEFITS

Risks

A potential risk of accidentally disclosing information regarding Washington University patients is possible though unlikely.

Benefits

The findings of the study will identify areas for improvement in antibiotic choice used for total knee arthroplasty and characterize intraarticular and serum antibiotic levels after standard use of intrawound antibiotics in cementless total knee arthroplasty.

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