The Eradication of Nasal Colonization of MRSA Using an Antimicrobial Clip

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1. Introduction

1.1 Backgrounds and Prior Research

The anterior nares of the nose act as a reservoir for the colonization of Methycillin Resistant Staphylococci aureus (MRSA). The incidence of colonization varies from 3-5% to as high as 30% depending on the population cultured. Because of the endemic risk for the development of an infectious disease associated with such colonization, the Commonwealth of Pennsylvania has made it mandatory that any patient admitted to the intensive care units of a hospital or from a skilled nursing facility be screened for nasal colonization of MRSA. Positive nasal cultures initiate the implementation of a protocol that includes isolation of the patient and the use of antimicrobial agents until the colonization is eradicated. Any elected procedures are deferred, as colonization of the anterior nares with MRSA is associated with a three-fold increase in surgical site infections. Existing protocols employ the use of isolation of the patient into a private room, the use of gowns, caps, gloves and masks for the personnel treating the patient and the application of nasal mupuricin twice a day for five days. If mupuricin is ineffective or the patient is allergic to mupuricin systemic antibiotics are employed. Problematic with this approach is that resistance to mupuricin continues to rise with it being effective in only 63% of the isolates and while the incidence of MRSA being isolated from infections continues to rise.

Recent research has shown that the use of nylon that has been processed in a proprietary manner enhances the inherent electrostatic charge and porosity of the nylon. The electrostatic attraction of the bacteria to the nylon facilitates the entry of the bacteria onto the clip where an antimicrobial bacterialcidal chemical reaction occurs. In vitro testing has resulted in complete killing of hospital and community strains of MRSA in eight hours. Reincubation of the plates revealed that the cidal effect continued for twenty-four hours.

1.2 Purpose:

The purpose of this research is to test the effectiveness of a nylon nasal clip in the eradication of nasal colonization of MRSA in a known population over a twenty-four-hour period. Serial cultures would also be obtained to assess the effectiveness over a period of time.
1.3  Rationale:

Hypothesis: If eradication of MRSA occurs in vitro because of the attraction of the bacteria to the clip, then the same attraction of nasal bacteria should occur in vivo. Once the attraction occurred the cidal effect of the clip would lead to elimination of the MRSA nasal colonization.

2. Study Objectives and Design

2. Primary Objectives

The primary objective of this research is to assess the effectiveness of a nasal clip placed into the anterior nares of the nose in eradication of nasal MRSA colonization over twenty four hours.

2.2  Secondary Objectives:

The secondary objective of this research would be to assess the number of MRSA colonies present in the nares prior to treatment.

2.3  Study Design:

The outpatient dialysis population with a known high incidence of nasal colonization by MRSA would be assessed using polymerase chain reaction (PCR) assays. Those showing positive PCR findings would undergo quantitative bacterial cultures to assess the spectrum of colony forming units. Once cultures were obtained subjects would be assigned to one of six groups (Groups I thru Group VI) in a consecutive order. Each of the six groups will have five subjects.

1) Application of a nylon nasal clip containing silver without normal saline nasal spray (Group I)
2) Application of a nylon nasal clip containing silver with normal saline nasal spray (Group II)
3) Application of a nylon nasal clip containing organosaline without normal saline nasal spray (Group III)
4) Application of a nylon nasal clip containing organosaline with normal saline nasal spray (Group IV)
5) Application of a nylon nasal clip without normal saline nasal spray (Group V)
6) Application of a nylon nasal clip with normal saline nasal spray (Group VI)

Placement of a nasal clip would occur and the clip would remain in place for twenty-four hours. Half of the subjects will use a normal saline nasal spray to facilitate bacterial migration. After removal of the nasal clip, repeat
quantitative cultures would be obtained. Correlation of the number of colony forming units obtained with the quantitative cultures will be made to assess the effectiveness of the clip on varying numbers of colony forming units over this period of time.

If persistent nasal colonization by MRSA was present after the removal of a clip the subject would be informed of the findings and would be offered an alternative treatment based on their nephrologists recommendations.

3. Study Population:

3.1 Sample Size:

A total of thirty dialysis patients that are PCR positive for MRSA will undergo quantitative cultures to determine the range of colony forming units in asymptomatic colonization. All thirty subjects will have an antimicrobial clip placed in their nose for twenty-four hours. All thirty subjects will undergo repeat quantitative cultures in twenty-four hours.

3.2 Inclusion Criteria:

1. The subjects must between the ages of eighteen and ninety.
2. Any female subjects of childbearing age must be on a proven method of birth control.
3. The subjects must have a positive nasal MRSA quantitative culture.
4. Agree to and have signed a consent to participate in the study.

3.3 Exclusion Criteria

1. A debilitating mental illness
2. On an antimicrobial medication for an infectious process.
3. Pregnancy
4. An allergy to any of the components of the nasal clip; silver, organosaline, nylon
5. Cold of flu like symptoms that would cause repetitive sneezing.
6. Subjects requiring the daily use of nasal antihistamine sprays.

3.4 Recruitment Process

A physician would recruit subjects who are undergoing outpatient renal dialysis. The nature, degree, and purpose of the study would be presented and explained to the participant. A signed and witnessed informed consent would be obtained by the principal investigator prior to enrollment and then the subject would be screened for MRSA nasal colonization using PCR technology. Once identified as a nasal carrier of MRSA the subjects would be
given the opportunity to participate in the study. The patient’s identity would be listed as an assigned number and no personal identifying information would be entered into the collection data.

3.5 Co Enrollment Guidelines

There are no Co Enrollment Guidelines for this study.

3.6 Participant Retention

Participants will remain in this study for a period of twenty-four hours after the removal of nasal clip. At this point repeat nasal quantitative cultures will be obtained. Once the final nasal culture is obtained the participants will be deemed completed.

3.7 Participants Withdrawal:

Participants will be withdrawn from the study if they are placed on a course of antimicrobials while the clip in place, develop a flu like syndrome that induces repetitive sneezing or nasal congestion, cannot tolerate the nasal clip or personally request to be removed from the study. Any information collected up to the point of the withdrawal will be retained and used for inclusion of statistical analysis.

4. Study Treatment/Product/Intervention

4.1 Treatment/Product/Intervention Formulation/Content

The nasal clip formulation is made from a medical grade nylon that has been used in existing medical devices. The clip’s porosity is created by the use of a blowing agent. A proprietary antimicrobial material, along with the blowing agent are infused into the nylon to allow for an even distribution of the blowing agent and the antimicrobial chemical. Scoring the outer portion of the clip expands the surface area of the clip. The clip has an external tab to facilitate placement of the clip. Once the clip is in place this tab is twisted and removed.

4.2 Treatment/Product/Intervention Regimen

The nasal clip is made in one size that fits into the anterior nares of adults and abuts the nasal septum. The same size clip will be used in all participants.

4.3 Treatment/Product/Intervention/Administration
Med-Dev, Inc. will be responsible for overseeing the manufacturing of the nasal clip to assure uniformity and consistency of the product. Med-Dev will be responsible for the packaging and sterility of the nasal clip. Med-Dec will be responsible for the delivery of the nasal clip to the Wound Institute & Research Center. The Wound Institute & Research Center will be responsible for placing the nasal clips and obtaining and collecting the nasal cultures. Clin-Micro Labs will be responsible for the PCR analysis, and both the quantitative and qualitative cultures.

4.4 Treatment/Product/Intervention Supply and Accountability:

All nasal clips will have an assigned lot number that will refer to the date of manufacturing, date of sterilization, and the nature and degree of the components employed in the manufacturing of the nasal clip.

4.5 Adherence Assessment:

Adherence to the protocol will be the responsibility of the Wound Institute & Research Center and any changes in the protocol will be at the discretion of the principal investigator who will submit proposed changes for their approval. No changes of protocol will be instituted without IRB approval.

4.6 Toxicity Management:

If in the opinion of the principal investigator that the participant is exhibiting a toxic, allergic or health care problem related to the placement of the nasal clip, cessation of the protocol will be initiated.

4.7 Concomitant Medications:

Enrolled study participants will be allowed to continue any and all concomitant medications. The use of antimicrobials will not be allowed.

5. STUDY PROCEDURES

5.1 Nasal Clip Selection:

All the nasal clips will be selected from the same lot number to insure uniformity and consistency. The lot number will be at the discretion of Med-Dev Inc.
5.2 Data Collection:

The culture reports will be collected by the Wound Institute & Research Center to assess their clinical significance. Once a clinical correlation has been made as to the significance of the findings, the information will be sent to Med-Dev, Inc. for statistical analysis.

5.3 Data Analysis:

Comparison analysis of in vitro findings to in vivo findings will be made as to the effectiveness of the clips ability to suppress colony forming units. Analysis of the quantitative cultures will be made to establish a database for the range of organisms that constitute colonization.

6 SAFETY MONITORING AND ADVERSE EVENT REPORTING

6.1 Safety Monitoring

The safety of the participants will be moderated by the clinical coordinator ensuring compliance with the protocol and would also be responsible for documenting and reporting any adverse events related to the study to the principal investigator.

6.2 Adverse Event Reporting Requirements

Adverse events include but are not limited to:

A single occurrence of a serious, unexpected event that is uncommon and strongly associated with the use of the clip.

A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with the use of the clip, but uncommon in the study population.

Multiple occurrences of an adverse event that, based on an aggregate analysis, is determined to be an unanticipated problem.

Any other AE or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator’s brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects.

The period during which adverse events will be documented and reported will be defined as the tie period between the patient’s initiation into the study and thirty days following discharge from the hospital.
6.3 Serious Adverse Event Reporting Requirements

A serious adverse event that is described or addressed in the investigator’s brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence will be considered unexpected for the purposes of reporting.

A serious adverse event (SAE) is any AE that is
- Fatal
- Life Threatening
- Requires or prolongs hospital stay
- A congenital anomaly or birth defect
- An important medical event

Any SAE will be reported within twenty four hours of its occurrence to the Principal Investigator:

Michael F. Moore, MD
Phone: (570) 961-8000
Fax: (570) 961-8007
E-mail mmooremd@managewounds.com

Any SAE will be reported to The Wright Center for Graduate Medical Education Institutional Review Board within forty eight hours of Principal Investigator’s knowledge.

Kenneth H. Rudolph, M.D., Chairman of the Wright Center for Graduate Medical Education Institutional Review Board
Phone: (570) 343-2383
E-mail: khrudolph@verizon.net.

7 STATISTICAL CONSIDERATIONS

7.1 Review of Study Design

The study is designed to evaluate the effectiveness of a nasal clip in the eradication of the nasal colonization of MRSA.

7.2 Endpoints

7.2.1 Primary Endpoint

The eradication of nasal colonization by MRSA
7.22 Secondary Endpoint
   The establishment of a data base concerning the number of colony forming units that constitute colonization.

7.3 Accrual, Follow-up and Sample Size
   The intended sample size is thirty participants.

7.4 Consecutive Assignment
   All participants will be assigned a nasal clip from the same lot number.

7.5 Blinding
   There will be no blinding of the personnel engaged in this protocol.

7.6 Data Analysis
   7.6.1 Primary Analyses
       McNemar’s test
   7.6.2 Secondary Analyses
       Paired t test analysis

8 HUMAN SUBJECTS CONSIDERATIONS

8.1 Ethical Review
   This study is to be conducted according to US and international standards of GCP (FDA) Title part 312 and International Conferences of Harmonization guidelines, applicable government regulations, and institutional research policies and procedures. This protocol and any amendments will be submitted to a properly constituted Review Board or Ethics Committee (EC) in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision to the principal investigator prior to the commencement of this study.
Subsequent to initial review and approval, the responsible IRBs/ECs will review the protocol at least annually. The Investigator will make safety and progress reports to the IRBs/ECs at least annually, and within three months of study termination or completion. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and all unanticipated problems involving risks to human subjects or others.

8.2 Informed Consent

Only after the patient has agreed to enroll in the study and has signed an informed consent will the patient be assigned a study number based on the criteria described in the study design. No patient will be enrolled in the study unless an informed consent has been obtained and witnessed by the principal investigator.

8.3 Risks

The risks of the study would be a local or systemic allergic reaction to the components of the clip. There is also the risk that the clip would be ineffective in controlling bacterial growth and that a local or systemic infection could develop.

8.4 Benefits

If on completion of this study it were found that the nasal clip leads to the eradication of colonization in the anterior nares the benefits to society would be a new treatment that does not employ antibiotics. This would lead to a diminution of bacterial resistance, decrease in allergic reactions. There would be the added benefit of a shorter treatment time and a decrease in nursing time.

8.5 Incentives/Compensation

A twenty five dollar ($25.00) stipend will be given to all those participants willing to undergo screening. Participants who are enrolled in the study will receive an additional twenty five dollar ($25.00) stipend at the conclusion of the study.

8.6 Confidentiality

All study-related information will be stored securely at the study site. All participant information will be stored in secured area with access limited to study staff. All local databases will be secured with password-protected access.
8.7 Study Discontinuation

The study also may be discontinued at any time by the US Food and Drug Administration, other government or regulatory authorities, and/or site IRBs/ECs.

8.8 Emergency Response Plan

In the event of an emergency, investigators and clinical staff will respond according to accepted medical practice and institutional procedures and in compliance with all applicable rules and regulations to ensure the safety of the study participants as well as the security of the data and records. Injuries possibly related to the study procedures and/or the nasal clip, including allergic reactions, will be treated according to the needs of the patient as determined by the patient’s physician. All treatment related to the injury will be accurately recorded and documented in the study records and reported to the IRB. Any infection that manifests in the patient population, whether associated with the patient’s underlying condition or the study procedures, or of an etiology unrelated to the study, will be treated in accordance with standard infection control and treatment and in compliance with institutional guidelines. Existing health insurance policies will cover the cost of any necessary treatment as a result of participation in the study.

9 LABORATORY SPECIMENS AND BIOHAZARD CONTAINMENT

9.1 Local Laboratory Specimens

All culture specimens will be collected by the Wound Institute & Research Center and sent to Clin-Micro for analysis

9.2 Central Laboratory Specimens

Not Applicable

9.3 Biohazard Containment

The Wound Institute & Research Center & Research Center will follow standard existing protocols for the containment and disposal of biohazard materials.

10 ADMINISTRATIVE PROCEDURES

10.1 Study Activation

Study Activation will begin with the approval of the IRB board governing the protocol.
10.2 Study Coordination

Coordination of the study will be performed by the Wound Institute & Research Center and Med-Dev, Inc. Med-Dev, Inc. will ensure the acquisition and delivery of the nasal clips to the Wound Institute & Research Center. The Wound Institute & Research Center will be responsible for the acquisition of the data, entry of the data, and statistical analysis of the data.

10.3 Study Monitoring

Study monitors from the Wound Institute & Research Center and Research Center will verify compliance with human subjects and other research regulations and guidelines; assess adherence to the study protocol, and confirm the quality and accuracy of information collected at the study site and entered into the study database.

Site investigators will allow study monitors to inspect study facilities and documentation (e.g., informed consent forms, clinic and laboratory records, other source documents, case report forms), as well as observe the performance of study procedures. Investigators will also allow inspection of all study-related documentation by authorized representatives US and in-country government and regulatory authorities. A site visit log will be maintained at the study site to document all visits.

10.4 Protocol Compliance

The study will be conducted in full compliance with the protocol. The protocol will not be amended without prior written approval by the Principal Investigator. All protocol amendments must be submitted to and approved by the relevant IRB(s)/EC(s).

10.5 Investigator's Records

The individual investigator will maintain and store in a secure manner, complete, accurate, and current study records throughout the study. Study records include administrative documentation — including protocol registration documents and all reports and correspondence relating to the study — as well as documentation related to each participant screened for and/or enrolled in the study — including informed consent forms, locator forms, case report forms, notations of all contacts with the participant, and all other source documents.
10.6 Use of Information and Publications

Publication of the results of this study will be governed by existing protocols of the Wound Institute & Research Center & Research Center and with the approval of Med-Dev. Inc. Any publication or presentation regarding the outcome of this study will not include the use of any patient information.

11. REFERENCES


