An Evaluation of the Use of DuraDerm® for the Reduction of Pin Track Infection in Research Participants Receiving External Fixation Following Deformity Correction and Traumatic Provisional Fixation

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Purpose of the Study

The purpose of this study is to determine if DuraDerm®, a medical device having novel technology, leads to a reduction in pin track infection rate (compared to the average prevalence reported in the literature) when applied as part of a pin track care protocol.

Background

Metal pins are commonly used for external fixation in research participants undergoing reconstructive or repair surgery. These pins protrude through the skin and create an avenue for migration of organisms. Anytime there is a break in the integrity of the skin, the risk of infection is increased. Pin site infections are a very common complication of external fixation, and unfortunately, the literature is scant on how to optimally minimize the risk of infection.

A Cochrane Collaboration Review published in 2004 to assess the effect on infection rates of different methods of cleaning and dressing orthopedic percutaneous pin sites determined that there was little evidence as to which pin site care regimen best reduces infection rates.[1]

Depending on the reference, pin track infections rates have been reported to range from 0% to 100%. A systematic review of the incidence of pin track infections associated with external fixation published in 2016 revealed a cumulative pin track infection rate of 27%. This rate was defined as the inherent risk of any given research participant developing a pin track infection at a random pin or wire site during the course of treatment with external fixation.[2] A 2016 review describes pin track infection as the most commonly expected problem, or even an almost inevitable complication, when using external fixation.[3]

Several limitations of the current literature pose significant barriers to the study of pin site infection preventative strategies.[4] Limitations include:

1. Lack of uniform definition/criteria to diagnose and classify severity of pin track infections. This makes it difficult to define the true incidence.
2. Highly variable control groups between studies. This creates difficulty in applying study results to an individual practice or protocol for preventative care.
3. Within studies, treatment groups often differ by more than one variable (e.g. changing both the cleaning solution and dressing type). This makes it impossible

to determine the effect of individual variables and applying study results to an individual practice for protocol.

4. There exists few randomized controlled trials. This creates clinical practice based on low quality, underpowered, potentially biased studies.
5. There is no consistency in reporting infection rate (per patient vs per individual pin site). This creates difficulty in studying incidence, comparing studies, or conducting an accurate meta-analysis.

Research participants eligible for the study will be those undergoing Deformity Correction and Traumatic Provisional Fixation. These research participants have a number of pins placed to ensure this required rigid fixation. The number of external fixation pins averages approximately ten per research participant.

DuraDerm® is a 510K FDA cleared medical device indicated for providing a covering over minor wounds and scrapes that are clean and dry. The microbicidal liquid solution consists of organic polymer dissolved in methylene chloride organic solvent. The unique formulation eradicates any organisms (bacteria, fungi, viruses) it comes in contact with. This is a result of the methylene chloride's activity against an infinite number of organisms. The methylene chloride evaporates leaving a clear, elastomeric, non-odorous film for covering minor wounds. The film protects the wound against entry of water, dirt, and germs. The film is elastomeric and protects in difficult regions where flexing, bending and creasing skin occurs. The clear film forms in less than a minute. Application is commonly accomplished using a cotton tip applicator. The liquid is applied on and around the wound extending at least an inch and a quarter beyond the edges of the wound. Momentary stinging may occur upon initial application. The film commonly remains intact for one to three days or longer depending on exposure to rubbing, flexing, or soap and water. This film is resistant to degradation by water alone, but can be easily removed with the combination of soap and water or it can be gently peeled off starting at the outer edges. DuraDerm® is for external use only. DuraDerm® is not intended for use on deep or infected wounds or puncture wounds, or for use near the eyes, mouth, or nose. Intentional inhaling of the contents may be harmful or fatal. The bottle should be tightly capped after each use to prevent evaporation of the solvent.[4]

The Principle Investigator has utilized topically applied DuraDerm® as an additional step in his current treatment protocol for pin site care for several research participants (approximately 25) with over 200 pin sites with only 2 pin site infections. This represents a significant reduction from the average incidence of pin site infections reported in the literature (<1% vs 27% on a per research participant basis).

This study will be undertaken to formally evaluate whether DuraDerm® used on pin sites leads to a reduction in pin track infections when compared to the reported average incidence in the literature.

Criteria for Research Participant Selection

- 6 research participants with approximately 60 pin sites (average 10/research participant) will be enrolled into the study for the Control group receiving standard pin track care.
- 6 research participants with approximately 60 pin sites (average 10/research participant) will be enrolled into the study for the DuraDerm® group. These research participants will receive the exact same standard pin track care with the addition of DuraDerm® applied at each cleaning of the pin track area, as an additional step in the pin track care protocol.

The age of research participants was chosen based on the majority of principle investigator's research participants being adults and to avoid any special consideration that may apply to research with minors. The study will not be gender specific. There are no enrollment restrictions based upon race or ethnic origin. Study protocol will continue post discharge up to 6 to 8 weeks until patient final visit post pin removal. Proper inserving of product was conducted and documented.

Inclusion Criteria:

1. Deformity correction, traumatic provisional fixation
2. All pin sites are stable
3. 18 years of age or greater
4. No known contraindication to receive DuraDerm®

Exclusion Criteria:

1. Age less than 18 years
2. Known allergy to Methylene Chloride
3. Known sensitivity to organic polymers
4. Non-clean, dry wound at pin
5. Vulnerable research participants (Institutionalized, students, employees, prisoners, or those with decisional incapacity, etc.)

Methods and Procedures

The study will enroll 12 total research participants (6 control research participants and 6 DuraDerm® research participants) with approximately 120 pin sites (approximately 60 in the Control group and 60 in the DuraDerm® group). Each research participant undergoing Deformity Correction and/or Traumatic Provisional Surgery will be asked to participate in the study to evaluate if the topical application of DuraDerm® as an additional step in the management of post-operative pin track site care reduces the incidence of pin track infections. Investigational Review Board (IRB) approval will be obtained and informed research participant consent will be obtained from each research participant.

For the control group, the usual care of pin track sites will be followed as outlined below (Pin Track Care Regimen). For the DuraDerm® group, the same care regimen will be followed with the addition of DuraDerm® applied topically to pin track site as the

experimental procedure being performed for research purposes. No additional tests or procedures outside of the existing standard regimen currently being utilized are anticipated.

Pin Track Care Regimen

Control and DuraDerm® Groups

All pins and wire sites will be cleaned daily while hospitalized. Basic pin care will be performed once daily by hospital nursing staff prior to discharge. Following discharge from the hospital, the pin care protocol will be continued by research participant's caregiver.

Ideally, pin sites are cleaned when the surrounding skin and gauze are soft. This should make removal of gauze and cleaning of pins less painful. The purpose of the cleaning is to prevent the skin from attaching to the pins and wires and to decrease the chance of infection, as well as, inspect the area for any signs of infection.

Research participants will be instructed to notify the Principal Investigator if they observe any signs or symptoms of infection. These include redness around pin site, discharge, tenderness in the soft tissue, loosening of the pin, nausea, vomiting, fever or chills.

Research participants will be instructed that the approach to pin care should occur in a step-wise fashion. If Step 1 is effective there is no need for further debris removal and research participants will be instructed conclude the care protocol (Control Group) or proceed to Step 3 (DuraDerm® group). Basically, if Step 1 removes all debris, Steps 2 is not necessary. It is not uncommon for all of Steps 1 and 2 to be needed to completely remove debris.

Step 1: Brush the pin sites with saline using an ordinary soft toothbrush or gauze with sterile gloves

Step 2: If following Step 1, debris remains, use forceps (tweezers) to gently remove debris.

DuraDerm® Group (IDENTICAL CARE AS DESCRIBED ABOVE + Step 3)

Step 3: Apply DuraDerm® with Q-tip on clean dry wound around (extending approximately one inch around pin site) and on the pin. DuraDerm® will be applied daily while in the hospital and then at a minimum of at least three times a week until pin removal.

DuraDerm® should be reapplied at the end of each Pin Care Cleaning Regimen.

See Attachment – Schedule of Events

Data Analysis and Data Monitoring

This is a prospective observational case series study to measure the potential reduction in pin track infection rate among research participants undergoing Deformity Correction and Traumatic Provisional Fixation.

Data will be collected by clinical staff under supervisor of the Principal Investigator. Data collected is primarily categorical and will be analyzed using tabulations (tables of frequencies), visual displays (histograms), and chi-square or Fisher exact tests to measure variable independence (e.g., infection rate based on age, number of pins/research participants, etc.).

Data Storage and Confidentiality

Data will be stored on Principle Investigator's computer which is secured by password protection. A hard copy backup with also be kept and be stored in a locked cabinet or office with limited access. Confidentiality will be maintained by assigning each research participant a unique research participant identifier. Research participant identifier will consist of research participant's initials and date of birth. Raw data will not be shared with anyone. Tabulated data with confidential research participant identifiers will only be shared with study coordinator and statistician.

Risk/Benefit Assessment

Risk Category

This research study presents minimal risk to the research participant. DuraDerm® has been used by over 3,000 individuals without any reported serious side effects

Potential Risk

The most common side effect of DuraDerm® is momentary stinging upon application. Intentional inhalation of the contents may be harmful or fatal. The product should be used with adequate ventilation. DuraDerm® should be kept away from children and not used near the eyes, mouth, or nose. The solution may be damaging to clothes or finished surfaces. If ingested, obtain medical assistance immediately. If used as directed, the probability of any potential risk is minimal. Since this study is being conducted on

extremity pin tracks, the application with be of significant distance from the eyes, mouth or nose. The only foreseen risk form the application of DuraDerm® on pin track sites is momentary stinging and this is not a consistent risk.

Protection Against Risk

All research participants will be monitored for potential redness or irritation at the pin track sites, and if any occurs, discontinuation of application may be warranted if it is believed to be a result of a reaction to the product. Any significant adverse event will be reported to the FDA utilizing FDA Medwatch Form 3500.

Potential Benefit to the Research participants

Since the infection rate of pin track research participants is approximately 27%, and initial information provided by the principle investigator indicates a much lower pin track infection rate, the benefit of reduced infection appears to significant.

Alternatives to Participation

Should a research participant elect not to participate in the study, they will receive standard pin track site care as described for the control group.

Research participant Identification, Recruitment and Consent Form

Method of Research Participant Identification, Recruitment and Consent/Assent

Research participants identified for the study will be those undergoing Deformity Correction and Traumatic Provisional Fixation who are under the care of the Primary Investigator. These research participants have a number of pins placed to ensure this required rigid fixation. The number of external fixation pins averages approximately ten per research participant. Research participants seen by the Primary Investigator who will be undergoing deformity correction or traumatic provisional fixation, will be invited to take part in this research study. No recruitment of the Principal Investigator's own students, employees, or family members will be allowed. Research participants who do not wish to participate in this randomized study will be provided the standard pin track care protocol this investigator utilizes for his research participants and will not have the opportunity to receive DuraDerm®.

Process of Consent

The Primary investigator and other key personnel on the study (fellow, nursing staff, intake coordinator and others) will be authorized to obtain consent from potential research participants for inclusion in the study. The process will be structured to present to the research participants the option to take part in this research that is intended to provide more conclusive information on the ability of DuraDerm®, a new liquid polymer

technology to reduce pin track infections. The potential research participants will be provided the consent form and this information will be explained to them. It will be made clear that participation in the study is completely voluntary and if they do not choose to take part in the study, they will receive the usual pin track standard of care provided by the Primary Investigator. The Primary Investigator or authorized team member will be responsible for signing as witness of consent being given.

Research Participant Capacity

All research participants will have the capacity to provide informed consent. If a research participant presenting to the Primary Investigator's practice, is not able to provide informed consent, they will not be presented the opportunity to take part in the study.

Research Participant/Representative Comprehension

If a research participant has been determined to be eligible for study participation based on the inclusion/exclusion criteria, they will be provided with the consent form and the information within the consent form will be discussed. Only those research participants indicating they understand the risks and benefits of receiving DuraDerm® as part of their pin track care protocol in the study and stating clearly that they would like to voluntarily participate, will be given the opportunity to take part in the study.

Debriefing Procedures

No information will be purposely withheld from the study research participants.

Consent Form

See attached.

Documentation of Consent

Consent will be documented on an individual consent for each research participant. These forms will be kept in a secure file cabinet in the Principal Investigator's office.

Cost to Research Participants

Research participants in this study will incur no additional costs for participation in the study. All DuraDerm® will be provided at no cost to the research participants in the DuraDerm® treatment group. No additional charges other than those normally occurring under the standard pin track care protocol will occur. All DuraDerm® will be provided by Prevent-Plus, LLC, the patent holder of DuraDerm®.

Payment for Participation

No payment or any other type of reimbursement will be provided to the research participants in this study.

See Consent Form – Attachment 1

See Data Collection Sheet –Attachment 2

References:

1. Temple J, Santy J. Pin site care for preventing infections associated with external bone fixators and pins. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.:CD004551. DOI: 10.1002/14651858.CD004551.
2. lobst CA, Liu RW. A systematic review of incidence of pin track infections associated with external fixation. *J Limb Lengthen Reconstr* 2016;2:6-16.
3. Ceroni D, et al. From Prevention of pin-tract infection to treatment of osteomyelitis during paediatric external fixation. *J Child Orthop* 2016;10:605-612.
4. Kazmers NH, et al. Prevention of pin site infection in external fixation: a review of the literature. *Strat Traum Limb Recon* 2016;11:75-85.
5. Sammarco VJ. Superconstructs in the treatment of Charcot foot deformity: plantar plating, locked plating, and axial screw fixation. *Foot Ankle Clin* 2009;14(3):393-407.