Study Synopsis

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**Infection rate and microbiological epidemiology of open fractures in the Solomon Islands and the impact of adjusted preemptive antimicrobial treatment on the infection rate - a prospective cohort study**

**1. Investigators**

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**2. Background**. Infection remains a serious problem for patients, surgeons and health systems in developed and in developing countries. In addition, orthopaedic trauma represents an increasing challenge globally. A strong argument against the use of modern orthopaedic surgical trauma care in low and middle income countries, apart from the cost of the implants and the lack of personnel, has been the fear of infection (Young 2013). However, there have been very few studies of good quality determining the infection rates after orthopaedic surgery and the microbiological epidemiology in developing countries. Standard preemptive therapy in the National Referral Hospital (NRH) in Honiara consists of a narrow spectrum antibiotic treatment with cloxacillin, not covering a significant number of expected environmental microorganisms (particularly gram-negative rods).

**3. Aims**. This trial aims at investigating the incidence, clinical and microbiological characteristics, the diagnostic approach, surgical and antimicrobial treatment and outcome of open fractures treated in the NRH. Further targets of this trial include the implementation of standardized collection of intraoperative tissue samples during fixation surgery. Generating information on the microbiological epidemiology of contaminated wounds potentially allows deduction of recommendations on the optimal preemptive antibiotic treatment to prevent infections after open fractures, which is of big interest especially when implants are used. In addition, carrying out this study is expected to establish or optimize the harvest and microbiological evaluation of intraoperative tissue samples in the institution. A further aim is to introduce a infection form to collect data on fracture-associated infections and to generate a comprehensive data base.

**4. Study design**. This is a prospective single center study, with a first observational phase, followed by a second, interventional phase and a third, postinterventional phase.

|  |  |
| --- | --- |
| Observational phase | Data collection: Implementation of an infection data collection form for all patients in the in- and outpatient setting. Collection of data (infection incidence, therapy and outcome of patients with open fractures) and standardized tissue samples (3 specimen) harvested at the site of fracture fixation and which are sent for microbiological examination |
| Analysis of obtained data and elaboration of an adjustment of the preemptive therapy in patients undergoing surgery for open fractures |
| Interventional phase | Administration of adjusted preemptive antimicrobial therapy in clinical practice. |
| Postinterventional phase | Analysis of effectiveness and costs.Analyze data of the infection data collection form and compare incidence, microbiology and outcome before and after adjustment of antimicrobial therapy. In addition, estimation of the additional cost expense. |
| Dissemination. Use the outcomes from this project to broadly disseminate the results-with publication and implementation into the antibiotic guidelines in other countries of this region. |

Adjustment of the standard antibiotic guidelines in open fractures

**Analysis** of the obtained data

**Intervention** Administration of adjusted preemptive antimicrobial therapy

**Analysis** of effectiveness and comparison of infection rate

**Observation**: collection of data on:

* infection rate
* causative agents
* therapy
* ? outcome

1 year

1 year

This study will be conducted over a two year period at NRH in Honiara, Solomon Islands. The study design is prospective interventional with a one-year observation period during which surveillance and data collection will be performed to determine the incidence and characteristics of infections occurring after open fractures. At the beginning of year 2, the antimicrobial therapy for patients undergoing reposition surgery after open fractures is adjusted according to the data collected.

**5. Inclusion criteria**. All patients ≥18 years of age with open fracture involving the femur, tibia, radius, ulna and humerus (see definition below), hospitalized at the NRH in Honiara during the trial period, who are treated with an open reposition at the institution.

**6. Exclusion criteria.** Closed fractures and fractures, which are treated conservatively are excluded from the analysis.

**7. Sample size**

Expected /estimated number of open fractures/year?-->Hermann Oberli (trauma data base)

**8. Ethical approval**

--> to be clarified by Stephen Kodovaru

**9. Definitions:**

**9.1 Open fractures**

Diagnosis of an open fracture is based on Gustilo and Anderson classification.

* Type I: clean wound smaller than 1 cm in diameter, appears clean, simple fracture pattern, no skin crushing.
* Type II: a laceration larger than 1 cm but without significant soft-tissue crushing, including no flaps, degloving or contusion. Fracture pattern may be more complex.
* Type III: an open segmental fracture or a single fracture with extensive soft-tissue injury. Also included are injuries older than eight hours. Type III injuries are subdivided into three types: Type IIIA: adequate soft-tissue coverage of the fracture despite high-energy trauma or extensive laceration or skin flaps.
* Type IIIB: inadequate soft-tissue coverage with periosteal stripping. Soft-tissue reconstruction is necessary.
* Type IIIC: any open fracture that is associated with vascular injury that requires repair.

**9.2 Infection (surgical site infection according to CDC)**

* **Superficial incisional infection**:
* Infection occurs within 30 days after the operation

*and*

* infection involves only skin or subcutaneous tissue of the incision

*and*

* at least *one* of the following:
* Purulent drainage, with or without laboratory confirmation, from the superficial incision.
* Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
* At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat *and* superficial incision is deliberately opened by surgeon, *unless* incision is culture-negative.
* Diagnosis of superficial incisional SSI by the surgeon or attending physician.
* **Deep incisional infection:**
* Infection occurs within 1 year if implant is in place and the infection appears to be related to the operation

*and*

* infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision

*and*

* at least one of the following:
* Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
* A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness, unless site is culture-negative.
* An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
* Diagnosis of a deep incisional SSI by a surgeon or attending physician.

**10. Data collection (see trauma and infection form):**

The following variables will be collected at admission in case of fracture:

* Demographics (age, sex)
* Date, location and type of fracture, circumstances of the accident
* Delay between accident and fixation surgery
* Type of fracture fixation, number of revisions, use of VAC
* Local conditions at first presentation
* Microbiology: tissue biopsy culture at first surgery and definitive stabilization (if applied); (incubated for 5 days (aerobic (and anaerobic) culture)
* Preemptive antibiotic treatment (substance, duration)
* Outcome (infection yes/no)

In case of infection, the following variables will be collected (see infection form (15))

* Demographics
* Infection diagnosis
* Location
* History (revision surgeries, septicaemia)
* Information on implant
* Diagnostics (clinical presentation, laboratory, imaging, microbiology)
* Treatment

**11. Follow up:**

Patients are evaluated at discharge (end of treatment), after 3 months and after 1 year (realistic?) or at unscheduled visits.

**12. Collaborating partners:**

- National Referral Hospital, Honiara, Solomon Islands

- Charité - University Medicine, Berlin, Germany

- Pro Implant Foundation

- Pacific Islands Orthopedics Association (PIOA)

- South Pacific Medical Projects

- *Which Australian Centers?*

**13. Literature (to be completed)**

1. **Young S, Lie SA, Hallan G, Zirkle LG, Engesaeter LB, Havelin LI.** 2011. Low infection rates after 34,361 intramedullary nail operations in 55 low- and middle-income countries: validation of the Surgical Implant Generation Network (SIGN) online surgical database. Acta Orthop **82:**737-743.

2. **Yusuf E, Steinrucken J, Buchegger T, Trampuz A, Borens O.** 2015. A descriptive study on the surgery and the microbiology of Gustilo type III fractures in an university hospital in Switzerland. Acta Orthop Belg **81:**327-332.

3. **Fehr J, Hatz C, Soka I, Kibatala P, Urassa H, Battegay M, Jeffrey Z, Smith T, Mshinda H, Frei R, Widmer AF.** 2006. Antimicrobial prophylaxis to prevent surgical site infections in a rural sub-Saharan hospital. Clin Microbiol Infect **12:**1224-1227.

4. **Young S, Lie SA, Hallan G, Zirkle LG, Engesaeter LB, Havelin LI.** 2013. Risk factors for infection after 46,113 intramedullary nail operations in low- and middle-income countries. World J Surg **37:**349-355.

**14. Budget estimation (in €):**

|  |  |  |  |
| --- | --- | --- | --- |
| **Item description** | **1st year** | **2nd year** | **Total** |
| Personnel costs |  |  |  |
| * Local study investigator – on-site study management, instruction, monitoring and data collection (500 €/month) | 6.000 | 6.000 | 12.000 |
| * International project coordinator – coordination and management (250 €/month) | 3.000 | 3.000 | 6.000 |
| * Microbiologist for on-site instructions and quality control assurance (20%) | 1.000 | 1.000 | 2.000 |
| * Data manager and biostatistics (outcome and expenses analyses) | 500 | 500 | 1.000 |
| * Local Study nurse / coordinator (250€/month) | 1.000 | 1.000 | 2.000 |
| Non-personnel costs |  |  |  |
| * Development of infection data collection form, documentation forms, archiving, mailing | 500 | 1.000 | 1.500 |
| * Microbiology consumables (growth media, susceptibility test kits, plastic ware, disinfectants, gloves etc.) | 5.000 | 5.000 | 10.000 |
| * Printing and dissemination costs | 500 | 2.000 | 2.000 |
| * Travel and accommodation expenses (for international project coordinator and microbiologist), 1 travel for 2 people/year = 4 travels for 2 years à 2.000€ | 4.000 | 4.000 | 8.000 |
| **TOTAL** | **21.500** | **23.500** | **44.500** |

**15. Infection form**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Demo-graphics  (analog trauma form) | Name:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Date of birth:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  ☐ outpatient ☐ admission | | | |
| Diagnosis (drop-down) | ☐ septic arthritis  ☐ acute osteomyelitis  ☐ chronic osteomyelitis  ☐ vertebral osteomyelitis/ spondylodiscitis | ☐ implant-associated infection  ☐ skin and soft tissue infection  ☐ necrotizing fasciitis  ☐ diabetic foot  ☐ other (Freitext) | | |
| Location  (analog trauma form) | ☐ Humerus ☐ R ☐ L  ☐ Ulna ☐ R ☐ L  ☐ Radius ☐ R ☐ L  ☐ Femur ☐ R ☐ L  ☐ Tibia ☐ R ☐ L  ☐ Malleolar ☐ R ☐ L  ☐ Clavicula ☐ R ☐ L  ☐ Spine ☐ C ☐ T ☐L  ☐ other: (Freitext)) ☐ R ☐ L | | Joints:  ☐ Knee ☐ R ☐ L  ☐ Hip ☐ R ☐ L  ☐ Shoulder ☐ R ☐ L  ☐ elbow ☐ R ☐ L  ☐ ankle ☐ R ☐ L  ☐ wrist ☐ R ☐ L  ☐ other ☐ R ☐ L | |
| history | ☐ open fracture (date :\_\_\_\_\_\_\_\_\_\_\_\_\_)  ☐ closed fracture (date :\_\_\_\_\_\_\_\_\_\_\_\_\_)  ☐ bite injury (date :\_\_\_\_\_\_\_\_\_\_\_\_\_)  ☐ surgery (date :\_\_\_\_\_\_\_\_\_\_\_\_\_; type of surgery: (Freitext))  ☐ intervention joint (aspiration, injection) (date :\_\_\_\_\_\_\_\_\_\_\_\_\_)  ☐ septicemia/ infection/ bacteremia: (date :\_\_\_\_\_\_\_\_\_\_\_\_\_)  ☐ surgery (date :\_\_\_\_\_\_\_\_\_\_\_\_\_; type of surgery: (Freitext))  ☐ other: (Freitext) | | | |
| implant | ☐ no  ☐ plate  ☐ screws  ☐ external fixator | ☐ nail  ☐ joint prosthesis  ☐ other: (Freitext) | | |
| Dia-gnostics | **clinical presentation:**  ☐ fever  ☐ pain  ☐ wound discharge  ☐ sinus tract | ☐ local signs of infection  ☐ exposed implant  ☐ other: (Freitext) | | |
| **Lab:**  ☐ ESR:\_\_\_\_\_\_\_\_\_mm/h ☐ CrP:\_\_\_\_\_\_\_\_\_\_ mg/L ☐ white blood count:\_\_\_\_\_\_\_\_\_\_ G/L  ☐ if joint aspirated: Leukocyte count:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_/uL | | | |
| **Imaging** method:  ☐ Xray  ☐ CT  ☐ sonogram | **Imaging** findings:  ☐ non-union  ☐ delayed union  ☐ abscess  ☐ osteomyelitis | | ☐ sequester  ☐ osteomyelitis  ☐ loose implant  ☐ other: (Freitext) |
| **Microbiology:**  ☐ S. aureus  ☐ Streptococcus sp.  ☐ Enterococcus sp.  ☐ E. coli  ☐ Enterobacter sp.  ☐ Bacillus sp. | ☐ coagulase-negative staphylococci  ☐ Pseudomonas sp.  ☐ Proteus sp.  ☐ Klebsiella sp.  ☐ Clostridium sp. | | ☐ fungi  ☐ Mycobacteria  ☐ Treponema sp. (syphilis, yaws)  ☐ other: (Freitext) |
| Treatment | **Surgical**  ☐ no surgery  ☐ debridement  ☐ wash out  ☐ amputation | ☐ removal of implant  ☐ exchange of implant  ☐ other: (Freitext) | | |
|  | **Antibiotics**  ☐ cloxacillin ☐ i.v. ☐ p.o. dosage: (Freitext)  ☐ amoxicillin/clavulanic acid ☐ i.v. ☐ p.o. dosage: (Freitext)  ☐ piperacillin/tazobactam ☐ i.v. ☐ p.o. dosage: (Freitext)  ☐ clindamycin ☐ i.v. ☐ p.o. dosage: (Freitext)  ☐ cotrimoxazol ☐ i.v. ☐ p.o. dosage: (Freitext)  ☐ ciprofloxacin ☐ i.v. ☐ p.o. dosage: (Freitext)  ☐ other: (Freitext)  ☐ duration (weeks): (Freitext) | | | |