Comparison of Honey and Povidone-iodine in Wound Healing on Acute Laceration Wounds: A Randomized Controlled Trial Study

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STUDY PROTOCOL

Objectives

Acute wound, where one of them is laceration wound, is a significant issue in the medical world due to its prevalence and quite a large treatment cost. Indonesia's national prevalence itself is 8.2%, with laceration wound ranked as the third top injury occurrence at 23.2%.[1] There is yet any data in Indonesia that shows how much cost is spent for the treatment of acute lacerations, although in U.S the total approximate cost per wound is $3927.[2] An acute open wound can potentially become a chronic wound, which causes more morbidity if not treated optimally.[3]

Choosing the appropriate wound dressing is one of the most important parts in the process of wound healing in order to reach an ideal condition.[3,4] Wound dressing usage in wide variety of healthcare services in Indonesia, is still limited to low-cost gauze dressing.[3] This may be caused by Indonesia's low gross domestic product per capita per month. In 2015, Indonesia is still classified as low-middle country compared to other countries which are $281.58 per person.[5,6] For East Nusa Tenggara province, the regional minimum wage and average per year in 2016 is still the lowest in Indonesia, which is Rp 1.425.000,- per person or an approximate of $ 97.74[7]

That particular income is not comparable to the total expense spent on wound treatment in the US. Meanwhile, in 2016 the *Indonesia Case Base Groups* (INA-CBG) consumers of the national health insurance encountered for wound care treatment in a type C hospital in regional 4 – where East Nusa Tenggara is listed in - is only a total of $ 12.96, which is very incomparable to the cost of modern wound dressing cost which ranges from $ 1.37 until $ 4.12.[8] Therefore, there is a need for an alternate wound dressing that can fulfill the ideal criteria without adding the patient's economic burden.

Povidone iodine is the most common wound dressing used in the area because of the benefits of low-cost, broad-spectrum efficacy, and it is safe for almost every type of skin and age. However, it does have the effect of delaying collagen synthesis, is toxic to fibroblast and keratinocyte, and also interferes with epithelial cell migration; every side effect that delays wound healing process makes its use on laceration wound controversial.[10]

In comparison to povidone iodine, honey has been used since a few centuries ago as medicine, especially for the treatment of chronic and even acute wound.[11] Honey can be a candidate for an antimicrobial agent on a wound dressing because of its antimicrobial, physiological mediator, and immunomodulatory effects. Compared to the conventional wound dressing, honey can accelerate the process of wound healing in partial-thickness burns.[12] On the contrary, honey has the risk of being contaminated by *Clostridium botullinum*.[10, 13] Until now, there have only been two journals that have compared honey and povidone iodine on chronic wounds. A study by Shukrimi A, et al stated that the duration of healing of an ulcer does not differ significantly on the use of honey and povidone iodine, with the average of 14.4 (7-26) days and 15.4 (9-36) days consecutively with $p < 0.005$.[14] Meanwhile, a study by Gulati S, et al stated that honey is superior to povidone iodine in 7 from 20 subjects given honey; where not 1 of the 20 subjects given povidone iodine attained perfect healing.[15]

Because until now there is no study that has compared the use of povidone iodine and honey on acute laceration wound, the investigators intend to implement a single-blind randomized control trial to compare both substances' effectiveness on acute laceration wound, especially in S.K Lerik General Hospital, Kupang. The evaluation parameters used are based on duration of wound healing, cleanliness of wound, odor, exudate level, pain, and itch of the wound. This study is anticipated to be one of the guidelines that is applicable in choosing a low-cost wound dressing capable to accelerate wound healing time, as well as convenient for the patient.

Design

Single-blind randomized control trial is used as the design for this study because of its effectivity and feasibility to assess the effects of honey in wound healing. In this study, single-blind masking is done on the participants where they do not know which intervention they have been given.

Methods

Our team consists of 5 members, each has their own tasks in S.K Lerik General Hospital's Emergency Room (when we meet the patient for the first time) and in the outpatient clinic (routine wound care). All of the data are primary. Data registry was taken by ourselves without involving other party members outside of the team. Any intervention done to the participants

were also done only by ourselves (suturing, wound care). Appointment for routine wound care was also done by ourselves by contacting the participant through their cell phone numbers which were collected when they came to the ER. The study started on 29th January 2018 and ended on 30th June 2018 until the least expected number of samples were collected.

The data of each participant was registered on a form, which was pre-made by our team. It recorded the identity of the patient, anamnesis, physical examination, and also to record more detailed information about our intervention, such as the number of stitches, and what kind of resources that we spent on the participant.

Every sample will be categorized into 3 randomized groups of intervention; honey, povidone-iodine, and paraffin gauze, which will also be categorized by location of their wound; face and neck, upper extremity, and lower extremity. The paraffin gauze was used as the standard care of wound dressing. Participants in each intervention group are distributed evenly using stratified block randomization. Photos of the wound will be taken both before and after the wound is cleaned, and after the wound has been sutured. Every patient will be asked to attend a predetermined schedule for wound care assessment. The wound will be evaluated by photos before and after the wound is cleaned, debrided, or have its sutures removed.

Every paper consists of participants' data that were collected on colored maps based on the intervention group (red: povidone-iodine, yellow: honey, blue: paraffin). At the end of the study, 3 members converted the data to be analyzed. We prepared beforehand the Standard Operational Procedures regarding any possibilities of adverse events, such as lidocaine toxicity and honey hypersensitivity.

We determined the sample size by ourselves since the amount of time is very limited, with the total sample of 36 participants, distributed evenly based on intervention groups and wounds' location. Both sexes are eligible, non-gender based, with age limit 10-60 years old. Moreover, the complete criteria are presented on Table 1 and 2.

There are two outcomes measured; the primary outcome and secondary outcome (Table 3). The primary outcome will be duration of wound healing per anatomical region. And the rest, such as infection, cleanliness of wound, odor, exudate level, pain, itch, and total cost of wound care, will

be considered as secondary outcome. Both are assessed per 2, 3, or 4 day interval, depending on each patient's wound timeline.

Table 1. The inclusion criteria for candidates.

Inclusion Criteria
Every patient that admits to the emergency department with: 1. An acute open traumatic wound 2. Agrees to a voluntary agreement for informed consent 3. To be treated in an outpatient setting

Table 2. The exclusion criteria consists of human factor and wound factor.

Exclusion Criteria:
Human factor: - Patient under the age of 10 and over 60 years old - Systemic conditions (diabetes mellitus, hypertension, liver & kidney disease) - Signs of infection - Consuming steroids and / or antibiotics - History of keloid - History of drug and / or alcohol abuse - Under treatment for chemotherapy or immunocompromised patient - Pregnant - History of allergy towards amoxicillin and / or ibuprofen
Wound factor: - Acute Open Traumatic Wound that has occured after than 12 hours of admittance to the emergency department - Open fracture - Suspicion of contamination from the mechanism of attaining the wound (human or animal bite, body fluids such as faeces, saliva, urine, sperm, or vaginal secretion) - Penetration trauma (stab wound, gunshot wound, or a joint-affected wound) - Signs of wound infection - More than one wound in the same anatomical region - Possess a chronic wound caused by underlying disease other than trauma - Wound with exposed tendon and/ or bone - Wound length dimension no less than 1 cm and no more than 10 cm. - Hypersensitivity to honey - Does not attend to scheduled wound care assessment control - Sample's wish to not be involved anymore with the research at any phase

Table 3. The outcome in admitted patient.

Outcume Measure
Primary Outcome Measure: 1. Wound healing time It is measured by days, when all of the sutures were completely removed. We followed the guideline from American Academy of Family Physicians for timing of suture removal, so as not to remove the suture before the recommended time. Secondary Outcome Measures: 1. Infection It is measured using the infection signs from Delphi criteria 3. Pain level It is measured using Numeral Rating Scale from 0-10, asked from the onset of the wound and every routine wound care 4. Itchiness It is measured using Numeral Rating Scale from 0-10, asked from the onset of the wound and every routine wound care 5. Odor It is measured using Verbal Rating Scale, consists of 4 level of odor (no odor, slight odor, medium odor, strong odor), asked from the onset of the wound and every routine wound care 6. Exudate It is measured in grams, using digital scale with the precision of 3 digits. We measured it from the gauze which will be used/on the wound, from the onset of the wound and every routine wound care 7. Cleanliness It is measured using images taken from the whole photographs of the wound. This parameter was measured using "less clean", "cleaner", "unchanged cleanliness". statistically using Cohen's kappa score to reach the agreement of the evaluation of this parameter 8. Cost It is measured by counting the cost of every material used for the participant

STATISTICAL ANALYSIS PLAN

Statistical analysis is performed using IBM SPSS Statistics 23 for Mac. After the data is collected, we will perform normality test using Shapiro-Wilk test for numerical data. Then variables are reported as means $\pm$ (standard deviation) or median (range), which depend on data's normality. Numerical data are analyzed using One Way Anova and ordinal data are analyzed using Kruskal-Wallis. Statistical significance is considered with a value of p less than 0.05.