Study Protocol with Statistical Analysis Plan

Official Title:
Optimizing Early Episiotomy Wound Healing: A Randomized Controlled Trial of Hydrophilic Methacrylate Gel Versus Beta-Sitosterol Ointment

Organization's Unique Protocol ID: MRC-01-23-518-EPIS

Underlying HMC Protocol Number: MRC-01-23-518

NCT Number: Not yet assigned (pending registration)

Document Date: December 4, 2025

Note: This protocol (MRC-01-23-518) covers both the episiotomy and cesarean-section strata of the parent study. This registration corresponds to the episiotomy stratum only.

HMC RESEARCH PROTOCOL

Study Title:	"Comparing the effectiveness of Hydrophilic Methacrylate Gel (Hemagel ®) and Beta Sitosterol Ointment in the Healing of Episiotomy and Cesarean Section Scars: A Randomized Controlled Trial"
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Amendment Summary Table	
Date of amendment	04/03/2024
After amendment	1-We will be blinding the tube ointments to ensure impartiality in the assessment of efficacy between the two treatments. This adjustment will enable us to minimize potential biases and ensure the integrity of our results. 2- Amending the timing of follow-up sessions from the initial plan of after 10 days to now occur on day 12, ensuring that follow-ups on days 5 and 12 align with weekdays and avoid any potential disruptions due to weekend days.
Before amendment	1-Due to the constraints of ointment differentiation, this trial will be open label. Both participants and healthcare providers will be aware of the allocated treatment group. 2-Next follow up on day 10
Location in the protocol	1-Under the section 7 (page number 8) "Study Population and Study Setting/Location" Subsection: "Blinding" 2- Under the section of "Methodology " subsection: Details of the interventions (not procedures) involved in the research (page 6)

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1. Synopsis

This RCT aims to assess the effectiveness of HM Gel (Hydrophilic Methacrylate Gel)and BS (Beta Sitosterol Ointment) in promoting the healing process of episiotomy andCS (cesarean section scars).

Episiotomy and cesarean section are common surgical procedures in obstetrics and gynecology, and scar healing is an important aspect of postoperative recovery. However, there is a lack of evidence comparing the effectiveness of topical treatments specifically for these types of scars. This study seeks to address this research gap by evaluating the effectiveness of Hydrophilic Methacrylate Gel and Beta Sitosterol Ointment in scar healing after episiotomy and cesarean section procedures.

The trial will employ a prospective, randomized controlled design. Adult females who have recently undergone episiotomy or cesarean section procedures will be recruited as participants, and informed consent will be obtained from each participant.

Participants will be randomly assigned to one of two groups: an experimental group receiving Hydrophilic Methacrylate Gel and a control group receiving Beta Sitosterol Ointment. The application of the respective treatments will follow established protocols.

Data collection will involve objective measures and participant-reported outcomes. Parameters such as wound healing progress, scar appearance, pain levels, and patient satisfaction will be assessed at predetermined intervals using standardized assessment tools and scoring systems.

Statistical analysis will be conducted to compare the primary and secondary outcomes between the two treatment groups. Appropriate statistical tests, such as t-tests or chi-square tests, will be employed to analyze the data.

The study will be conducted in adherence to HMC ethical guidelines, ensuring participant safety, privacy, and confidentiality.

The findings of this study will provide valuable insights into the effectiveness of Hydrophilic Methacrylate Gel and Beta Sitosterol Ointment in promoting the healing of episiotomy and cesarean section scars. The results may guide healthcare professionals in selecting optimal topical treatments for scar management, ultimately improving patient outcomes and satisfaction in the context of these surgical procedures.

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2. Abbreviations and Acronyms

RCT: Randomized Controlled Trial
HM Gel: Hydrophilic Methacrylate Gel
BS Ointment: Beta Sitosterol Ointment
CS: Cesarean Section
HMC: Hamad Medical Corporation

3. Introduction / Background

Episiotomy and cesarean section (CS) are common surgical procedures in obstetrics and gynecology, often performed to safeguard the well-being of both mothers and newborns (1). Adequate wound healing and effective scar management are vital components ofpostoperative care, profoundly influencing patient recovery, comfort, and long-termquality of life (2). However, despite the significance of these aspects, the current body of literature presents a noticeable gap in real-world evidence regarding the effectiveness of topical treatments specifically tailored for post-episiotomy and CS scars.

The absence of well-established treatment protocols, coupled with the limited researchin this area, presents significant challenges for healthcare professionals tasked with selecting the most suitable interventions for scar management. Current standard practices typically involve the use of emollients, moisturizers, and silicone-based products (3). However, the empirical evidence supporting their efficacy in promoting wound healing and enhancing patient satisfaction remains inconclusive (4, 5).

In the specific context of Al-Wakra Hospital, we conduct an average of approximately 350 deliveries each month, which includes both cesarean sections and normal deliveries with episiotomy procedures. This significant volume of procedures highlights the relevance and importance of investigating the most effective scar management interventions.

In our standard clinical practice at Al-Wakra Hospital, emollient, moisturizer such as betasitosterol is commonly used for scar management.

The local healthcare system in Qatar and Al-Wakra Hospital is committed to providingthe highest standard of care to its diverse patient population. Given the substantial number of patients undergoing episiotomy and cesarean section procedures, optimizing scar management is imperative to improve patient outcomes and enhance overall healthcare quality.

The present research seeks to bridge this knowledge gap by conducting a rigorous clinical trial to evaluate the potential benefits of novel scar management interventionsfor post-episiotomy and CS scars. In particular, this study focuses on the effectiveness of Hemagel Ointment, a topical hydrophilic methacrylate gel that has demonstrated promise in wound healing and scar management across various clinical settings (6). Hemagel's hydrophilic nature allows it to create a moist wound environment, which aligns with established principles of wound healing (7).

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Additionally, its mechanism of action involves the formation of a protective barrier over the wound site, potentiallyreducing infection risk and facilitating a controlled healing process (8). While some studies have explored the application of Hemagel Ointment in wound healing, its specific effects on post-episiotomy and CS scars remain relatively uncharted territory. Consequently, there exists a compelling need to conduct well-designed clinical trials that rigorously assess Hemagel Ointment's efficacy and safety in the context ofthese surgical procedures.

Therefore, the aim of this study is to evaluate the effectiveness and safety of Hemagel Ointment in post-episiotomy and cesarean section scar care through a randomized clinical trial. This trial will provide comprehensive evidence regarding the effectivenessof Hemagel Ointment in promoting wound healing, alleviating pain, improving scar appearance, and enhancing patient satisfaction in these specific contexts.

By conducting a rigorous randomized clinical trial, we seek to generate high-quality data that will inform clinical practice and guide healthcare professionals in selecting optimal interventions for scar management in post-episiotomy and cesarean section cases. This research will contribute to the existing body of knowledge in scar care and providevaluable insights for healthcare professionals, ultimately improving patient outcomes.

The results of this study have the potential to facilitate evidence-based decision-making, facilitate personalized patient care, and potentially reduce the burden of complicationsassociated with post-episiotomy and cesarean section scars. Furthermore, the findings will contribute to advancing the field of scar management and may pave the way forfuture research and the development of targeted interventions.

4. Objectives

1- The primary objective of this trial is to evaluate the effectiveness of Hemagel Ointment in promoting wound healing and reducing complications among patients who have undergone episiotomy or cesarean section procedures. The assessment of wound healing will be conducted using a validated assessment tool, which is included as an attachment.

2- The secondary objectives of this study involve assessing the impact of Hemagel Ointment on pain management, scar appearance, and patient satisfaction. To measure pain levels, standardized pain scales will be utilized, allowing for a

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comparison of the effectiveness of Hemagel Ointment in alleviating pain compared to the control group. Furthermore, scar appearance will be evaluatedusing the Patient and Observer Scar Assessment Scale (POSAS), which is a validated tool designed to assess cosmetic outcomes. Patient satisfaction will be assessed through questionnaires, which are provided as an attachment.

Additionally, standardized pain scales will be employed to assess pain levels, and the attached scale provides further details on this measurement.

5. Indicate if this is a retrospective data review

- ☒ **Prospective study**

Provide the date range of the chart review: RCT

6. Study Methodology

The proposed study is a prospective, randomized controlled trial (RCT) that aims tocompare the effectiveness of two topical treatments, HM Gel (Hydrophilic Methacrylate Gel) and BS Ointment (Beta Sitosterol Ointment), in promoting the healing process of episiotomy and cesarean section scars. The study will include two groups: an experimental group receiving HM Gel and a control group receiving BS Ointment.

Sample size calculation or justification of numbers: A priori sample size calculationwill be conducted to determine the required number of participants for adequate statistical power. This calculation will consider factors such as the expected effect size, desired level of significance, power of the study, and anticipated dropout rate. We aim to recruit enough participants to ensure the statistical validity and generalizability of the study results.

The sample size for this study was determined based on the desired level of statistical power (80%) and the significance level (0.05). Since no prior estimates of effect size were available, a moderate effect size was assumed. Using a two-sample t-test, the sample size per group was calculated to be 53 participants in patients with cesarean section. Considering rounding up to the nearest whole number, a total sample size of

106 participants was determined for the 2 groups of cesarean section, and the same number for patients (53) with episiotomy, a total of 106 participants was determined for the 2 groups of vaginal delivery with episiotomy. This sample size calculation ensuresthat the study will have sufficient power to detect meaningful differences in pain levels and wound healing outcomes.

Dropout Rate:

The anticipated dropout rate is indeed an important consideration in sample size determination. We recognize the potential for participant attrition during the course of our study. To

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address this concern and to ensure the robustness of our findings, we have factored in an anticipated dropout rate of 10% in our sample size calculation. While this rate is conservative and aligned with similar clinical trials, we understand the importanceof minimizing the impact of dropout on our study's outcomes.

Sample Size Adjustment:

To further enhance the reliability of our results and address the concern regarding sample size, we have considered increasing the sample size slightly. By recruiting approximately 60 patients per group, we aim to provide against dropout-related issuesand enhance the generalizability of our findings. This adjustment allows for a more robust study design without compromising the practicality of recruitment within our study timeline and available resources.

Details of the interventions (not procedures) involved in the research:

The study involves the application of two topical treatments, HM Gel and BS Ointment,to the respective treatment groups. The application of these treatments will follow established protocols. The study does not involve any invasive procedures.

The administration of the assigned treatments will be administered in routine clinicalpractice following the surgical procedure, either episiotomy or cesarean section, and continue for a period of two weeks. During this period, the participants will be instructed on the proper application of the treatments. The application frequency and dosage willbe as follows:

- Hydrophilic Methacrylate Gel (HM Gel): Participants in the experimental groupwill be instructed to apply HM Gel to the surgical site two times a day, in the morning and evening, for the duration of the two-week treatment period.
- Beta Sitosterol Ointment (BSO): Participants in the control group will be instructed to apply BSO to the surgical site two times a day, in the morning and evening,also for the duration of the two-week treatment period.
- The application process will be explained to each participant, emphasizing the importance of consistent and thorough application. Adherence to the treatment regimenwill be monitored through regular follow-up visits. These follow-up visits will coincide with the baseline assessment, occurring at recruitment, and subsequent visits at Day 5and Day 12 postpartum. The administration of the assigned treatments will commence immediately following the surgical procedure, either episiotomy or cesarean section, and continue for a period of two weeks. During this period, the participants will be instructed on the proper application of the treatments. The application frequency and dosage will be as follows:
- Hydrophilic Methacrylate Gel (HM Gel): Participants in the experimental groupwill be instructed to apply HM Gel to the surgical site two times a day, in the morning and evening, for the duration of the two-week treatment period.

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- Beta Sitosterol Ointment (BSO): Participants in the control group will be instructed to apply BSO to the surgical site two times a day, in the morning and evening,also for the duration of the two-week treatment period.
- The application process will be explained to each participant, emphasizing the importance of consistent and thorough application. Adherence to the treatment regimenwill be monitored through regular follow-up visits. These follow-up visits will coincide with the baseline assessment, occurring at recruitment, and subsequent visits at Day 5and Day 12 postpartum.
- Phone Call Reminders by a trained staff to assess adherence of application. (Script is added in documentation in ABHATH)

Follow-Up Phone Calls:

Phone call reminders will be made by trained staff to assess treatment adherence. Specific timepoints for planned follow-up phone calls are Day 3 and Day 7.

These follow-up calls will serve to reinforce proper application, address any concerns,and ensure consistent adherence to the treatment regimen. The detailed script in the ABHATH documentation provides guidance for the phone call reminders.

Data/samples (bio-specimens/information) collected at each time point and why:

Data collection will involve both objective measures and participant-reported outcomes. The data to be collected at each time point include:

- Wound healing progress: This objective measure will assess the healing processof the scars over time.
- Scar appearance: This will be evaluated using the Patient and Observer Scar Assessment Scale (POSAS), a validated tool designed to assess cosmetic outcomes.
- Pain levels: Standardized pain scales will be employed to assess pain levels, comparing the effectiveness of the treatments in alleviating pain.
- Patient satisfaction: Questionnaires will be used to gather information on patient satisfaction with the treatment outcomes.
- These data will provide valuable insights into the assessment of the effectiveness of the treatments and their impact on wound healing, scar appearance, painmanagement, and patient satisfaction.

Risks to participants in the proposed research and anticipated benefits to clinical/health outcome:

As described, the proposed research involves the use of topical treatments (HM Geland BS Ointment) for wound healing and scar management. Both treatments are generally considered safe, and no invasive procedures are involved in the study.

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The anticipated benefits to participants include improved wound healing and scar appearance, reduced pain levels, and potentially enhanced patient satisfaction with the treatment outcomes. By comparing the two treatments, the study aims to provide evidence-based recommendations for scar management after episiotomy and cesarean section procedures, which may improve patient care and outcomes in these surgical contexts. The risks to participants are minimal, and the potential benefits to clinical and health outcomes make the research reasonably worthwhile.

7. Study Population and Study Setting/ Location

This study will be a prospective, randomized, controlled clinical trial. Participants will be randomly assigned to either an experimental group receiving HydrophilicMethacrylate Gel (HM Gel) or a control group receiving Beta Sitosterol Ointment(BS Ointment). The randomization process will utilize a stratified randomization method based on age and BMI to ensure balanced representation of different age groups and BMI categories within each treatment group.

Stratification:

In our study, we will indeed have two distinct groups of patients: those who have undergone episiotomy and those who have undergone cesarean section. We recognize that the type of surgery is a potentially important factor that should be considered in the randomization process to ensure balanced representation of both surgical groups in each treatment arm. To address this concern, we will implement a stratified randomization approach that accounts for the type of surgery as a stratification factor. Specifically, during the randomization process, participants will be stratified into two groups: the episiotomy group and the cesarean section group. Within each of these strata, randomization will be performed independently to allocate participants to either the experimental group receiving Hydrophilic Methacrylate Gel (HM Gel) or the control group receiving Beta Sitosterol Ointment (BS Ointment). In our final study report, we will provide a detailed description ofthe randomization process, including how participants were allocated to treatmentgroups within each stratum.

Blinding:

We will be blinding the tube ointments to ensure impartiality in the assessment of efficacy between the two treatments. This adjustment will enable us to minimize potential biases and ensure the integrity of our results.

The ointment tubes will be packaged in identical outer packaging, such as opaque boxes, to conceal any distinguishing features.

This approach will ensure that the participants nor the assessors of wound know which

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ointment is being used.

In addition, to minimize bias during data analysis, the data analysts will be blinded to the treatment allocation until the analysis is completed.

Informed Consent:

Informed consent is a crucial part of this study. We will carefully explain the details of the research to each participant, ensuring they have a comprehensive understanding of what is involved. This includes information about the nature oftheir participation, possible risks, anticipated benefits, and their right to withdraw from the study. Additionally, as a token of appreciation for their valuablecontribution, participants will receive a small encouragement gift. Our aim is toprovide participants with all the information they need to make an informed decision about their involvement in the research.

Study Duration:

The expected length of the study is one year (15/12/2023 - 01/11/2024), whichincludes participant recruitment, intervention, follow-up, and data analysis.

Study instruments :

To ensure the validity and cultural appropriateness of the study instruments, we will review the available literature and consult with experts in the field to identify validated instruments that have been culturally adapted for use in Arabic and other commonly spoken languages in Qatar. If such instruments are available, we will incorporate them into our study. In the event that validated instruments are not readily available in the desired languages, we will try to undertake a careful process of cultural adaptation.This process will involve translation, back-translation, and cognitive interviewing to ensure that the instruments are linguistically and culturally appropriate for ourparticipants.

Inclusion Criteria:

Eligible participants for this study will be adult females aged 18 years and above, who have recently undergone episiotomy or cesarean section procedures. Specific inclusion criteria include:

1. Adequate reading and writing literacy.
2. Live term singleton pregnancy.
3. Mediolateral episiotomy without tear.
4. Absence of chronic systemic diseases that delay wound healing (e.g., coagulation disorders, diabetes, anemia (Hb) < 9 g/dl).
5. No history of previous injury, surgery, or visible lesions in the perineum (e.g., genital warts, hemorrhoids).

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6. Does NOT have chorioamnionitis and/or postpartum endomyometritis
7. No manual removal of placenta.
8. No postpartum hemorrhage (PPH).
9. Absence of perineal hematoma.
10. Infant weight between 2500 and 4000 g.

Exclusion Criteria:

1. Use of other supplements or medications for wound healing during the study.
2. Inability to apply the ointment correctly as per instruction.
3. Sensitivity or allergy to the ointment or its components.
4. Participants who have a history of adverse reactions to similar topical treatments.
5. Participants who are unable to comply with study procedures and follow-up visits.

Note : The assessment of participants use of other supplements or medications duringthe study will be conducted through a combination of self-reporting and verification during regular follow-up visits. Participants will be asked to disclose any additionalsupplements or medications they are using, and this information will be cross-checked with their medical records in Cerner. Additionally, healthcare providers will activelyinquire about any changes in medication or supplementation during follow-up visits.

Data Collection:

Data collection will involve objective measures and participant-reported outcomes. The assessment will include wound healing progress, scar appearance, pain levels, and patient satisfaction. These parameters will be assessed at predetermined intervals using standardized assessment tools and scoring systems.

Sample Size Calculation:

A sample size calculation has been performed to determine the required number of participants in each age and BMI stratum based on the expected effect size and statistical power.

Study Location:

This study will take place at Al-Wakra hospital.

8. Study procedures

We plan to start the study as soon as MRC approval is obtained, and MRC approval letter is issued. The expected length of the study is one year.

Following MRC approval, we will start to stratify and recruit the patients based on inclusion

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and exclusion criterias . A research code (e.g. YK001) will be assign topatient to ensure privacy. A separate sheet will be kept with the PI including identifier date for each code). One of the investigators will then record the patients for inclusion. They will then be assigned the subject number code and the study variables will be recorded in a separate excel file under the patient's subject code.

- Study is expected to last 12 months (01/11/2023 -01/11/2024).

Timeline:

- Submission and approval of study (2 months)
- Data collection, cleaning, and analysis (5 months)
- result collation, interpretation, writing of manuscripts and dissemination (5 months).

Informed Consent

Yes (attached)

9. Risk

All collected data will be coded so as to avoid any risk of confidentiality breach.

Here are some potential anticipated risks to consider:

- Allergic reactions: Some participants may experience allergic reactions to the topical treatments, HM Gel, or BS Ointment. Allergic reactions can range from mild skin irritation to more severe symptoms, such as rash, itching, or swelling.
- Skin irritation: As with any topical treatment, there is a possibility of skin irritation at the application site. Participants may experience redness, itching, or discomfort around the wound area.
- Delayed wound healing: There is a small possibility that the application of the treatments may interfere with the natural wound healing process, leading to delayed wound closure or complications in some participants.
- Unsatisfactory scar appearance: Despite the use of the treatments, some participants may not achieve the desired cosmetic outcomes in scar appearance.This could potentially impact patient satisfaction with the treatment.
- No treatment effect: It's possible that neither treatment (HM Gel or BS Ointment) may demonstrate a significant effect on wound healing or scar management, leading to no substantial improvement in the participants' conditions.

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- Infection: Although both treatments are topical and not invasive, there is still a small risk of infection at the wound site due to various factors, such as inadequate wound care or microbial contamination.

Participants will be informed of these potential risks during the informed consent process, allowing them to make an informed decision about their participation in the research.

Bio-Specimens & Sample Collection

Not applicable

Outcomes

1- The primary outcome of this trial is to assess the effectiveness of Hydrophilic Methacrylate Gel (Hemagel) in promoting wound healing and reducing complications in patients undergoing episiotomy or cesarean section procedures. Specifically, we aim to compare the rate and quality of wound healing betweenthe group receiving Hemagel Ointment and the control group.

2- The secondary outcome includes evaluating the impact of Hydrophilic Methacrylate Gel on pain management, scar appearance, and patient satisfaction. We will assess pain levels using standardized pain scales and compare the effectiveness of Hemagel Ointment in alleviating pain compared to the control group. Additionally, scar appearance will be evaluated using validatedassessment tools to determine if Hemagel Ointment leads to improved cosmetic outcomes. Patient satisfaction will be assessed through questionnaires to gaugethe subjective experience and level of satisfaction with the treatment.

By achieving these objectives, this trial aims to provide evidence regarding the effectiveness of Hydrophilic Methacrylate Gel in promoting wound healing, managing pain, improving scar appearance, and enhancing patient satisfaction in the context of post-episiotomy and cesarean section scar.

Data Collection & Confidentiality

The patients name, medical record number and subject number will be recorded in a separate file. This file will be kept on a password locked computer at PIs office at pharmacy department of Al Wakra hospital.

The assigned subject number will be used to record all the study variables. No physical copies will be used and data will not be shared outside HMC.

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The principal investigator will control access to this study's data.

Once patients are chosen, Cerner database will be reviewed for details pertinent to the study.

The data will be collected as per the data collection sheet, which is attached for review. The PI is the one to collect the data in excel sheet and stored in a soft copy.

Access for data collected will be under control of the principal investigator.

Data will be collected de-identified, codes will be used to cover patient identifiers suchas Name, HC no., DOB. Any link between code and identifier will be deleted at the end

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of the data collection and anonymized data will be kept for at least 5 years after study completion.

Following MRC approval, a research code (e.g. YK001) will be assign to patient to ensure privacy. A separate sheet will be kept with the PI including identifier date for each code). One of the investigators will then record the names and medical record numbers of the patients for inclusion. They will then be assigned the subject number code and the study variables will be recorded in a separate excel file under the patient's subject code.

The linking sheet to the subject's identifier will be kept in a secure locked place in the PI office and will be destroyed after data collection and will not be shared outsideHMC. Data have to be stored for 5 years post study completion.

Subject Withdrawal/ Withdrawal of Consent

In this study, participants have the right to withdraw from the trial at any time without providing a reason. Withdrawal of consent will not affect their current or future medical care. Participants who decide to withdraw from the study will be informed that they are free to do so without any negative consequences. Their decision to withdraw will be respected, and their data collected up to the point of withdrawal will be retained and included in the analysis, unless they specifically request their data to be removed.

To ensure proper handling of participant withdrawal, the study team will clearly communicate the withdrawal process during the informed consent process. Participants will be provided with contact information for the study coordinator or principal investigator, who will be available to answer any questions or concerns related to the study or the withdrawal process.

If a participant decides to withdraw their consent, their study participation will be terminated immediately. Any unused investigational product (HM Gel or BS Ointment)will be collected, and no further assessments or interventions will be performed on the participant.

The reasons for withdrawal, if provided voluntarily by the participant, will be recordedto inform the study team of potential issues and ensure continuous improvement of the research process.

Participant confidentiality will be strictly maintained throughout the study and beyond. All data obtained from participants who withdraw their consent will be handled withthe utmost confidentiality and will not be disclosed in any study-related publications or presentations.

It is important to emphasize that participant withdrawal is entirely voluntary, and participants will be assured that their decision will not impact their relationship with the

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healthcare providers or Al-Wakra hospital in any way. Their safety and well-being will remain a top priority throughout the study, regardless of their decision to continue or withdraw from the trial.

10. Statistical Consideration and Data Analysis :

Randomization and Allocation Concealment:

We will be blinding the tube ointments to ensure impartiality in the assessment of efficacy between the two treatments. This adjustment will enable us to minimize potential biases and ensure the integrity of our results.

The ointment tubes will be packaged in identical outer packaging, such as opaque boxes, to conceal any distinguishing features.

This approach will ensure that the participants nor the assessors of wound know which ointment is being used. Blinding of data analysts will help ensure impartiality during the analysis process.

Randomization: We will indeed use computer-generated random numbers or randomization software to ensure unbiased and unpredictable allocation. Instead of stratifying during randomization, we will collect comprehensive data on age group, BMI, and type of surgery. Subgroup analyses will be conducted during data analysis, allowing for a thorough examination of treatment effects within specific subgroups.

Statistical Analysis Plan:

The statistical analysis plan will be as follows:

- Descriptive Statistics:
  Descriptive statistics will be used to summarize the demographic and baseline characteristics of the participants in both groups. Continuous variables, such as age and BMI, will be presented as means with standard deviations or medianswith interquartile ranges, depending on their distribution. Categorical variables,such as parity and type of surgery, will be summarized as frequencies and percentages.

- Primary Outcome Analysis:
  The primary outcome of wound healing will be analyzed using appropriate statistical methods. As the wound healing outcome is likely to be a categorical variable (e.g., healed/not healed), we will employ the chi-square test or Fisher's exact test, depending on the expected cell frequencies, to compare the proportions of healed wounds

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between the two treatment groups.

- Secondary Outcome Analysis:
  For secondary outcomes, such as pain management, scar appearance, and patient satisfaction, we will use similar statistical methods. Pain management and patient satisfaction may be assessed using standardized pain scales and questionnaires, respectively. Depending on the distribution of the data, we will utilize t-tests or Mann-Whitney U tests to compare continuous variables and chi- square tests or Fisher's exact tests for categorical variables.

- Intention-to-Treat (ITT) Analysis:
  The primary analysis will be conducted on an intention-to-treat (ITT) basis, including all randomized participants. This approach accounts for protocoldeviations and maintains the randomization balance between the groups. Participants will be analyzed according to their allocated treatment group, irrespective of protocol adherence or completion.

- Subgroup Analyses:
  We will perform subgroup analyses to explore potential effect modifiers, such as age, BMI, or parity, on the treatment outcomes. Interaction tests or stratifiedanalyses may be employed to investigate the impact of these factors on theprimary and secondary outcomes.

- Statistical Software:
  All statistical analyses will be performed using a reputable statistical software package, such as SPSS or R. These software tools are widely used for data analysis and will provide reliable results for this study.

- Statistical Significance:
  Statistical significance will be defined as a p-value less than 0.05. Results with p-values less than this threshold will be considered statistically significant, indicating a significant difference between the treatment groups.

- Who Will Perform the Analysis:
  The data analysis will be carried out by qualified statisticians Dr.Prem (HMC biostatician) with expertise in statistical methods. These individuals will be independent of the study's clinical team and will be blinded to the treatment allocation to ensure unbiased analysis.

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11. Adverse Event Reporting

Monitoring and Reporting of Adverse Events:

We will implement a systematic monitoring and reporting process to promptly identifyand assess adverse events throughout the study. The following steps will be followed:

-Participant Education: Participants will be provided with clear instructions on how to recognize and report any potential adverse events they may experience during the study. They will be informed about the importance of timely reporting and the methods for contacting the study team.

-Documentation: All adverse events reported by the participants or observed by the study personnel will be documented in detail. This documentation will include the natureof the event, date and time of occurrence, severity, duration, related symptoms, and any actions taken.

-Classification and Severity Assessment: Adverse events will be classified and assessedfor severity according to predefined criteria. The severity levels may include mild, moderate, or severe, based on the impact on the participant's well-being and the need for medical intervention.

-Causality Assessment: Adverse events will be evaluated for their potential relationshipto the investigational product (Hemagel Ointment) or other study procedures. Causality assessments will consider factors such as temporal association, known side effects of the product, and the presence of alternative explanations.

-Reporting and Follow-up: Adverse events of moderate to severe intensity or those considered related to the investigational product will be promptly reported to the principal investigator and the relevant ethics committee or institutional review board (IRB). The reporting will include a comprehensive description of the event, its severity,the participant's characteristics, and any actions taken or planned.

We will ensure that the reporting timelines align with the revised version of IRB SOP 09, available on the Abhath download center. Specifically, Serious Adverse Events (SAE) will be reported within 7 days, and any other unanticipated problems will be reported within 14 days.

We are committed to ensuring the highest standards of participant safety and ethicalconduct throughout the study.

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- Follow-up and Documentation: Adverse events will be closely monitored and followedup until resolution or stabilization. The progress and outcomes of the adverse events, including any necessary medical interventions or treatments, will be documented in the participant's records.

12. Ethical Consideration

The study will only be conducted after review and approval from MRC.

The study will be conducted in full conformance with principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of MoPHin Qatar."

13. Sponsor, Funding & Collaborator Information

Not applicable

14. Dissemination of Results and Publication policy

Once the study is completed it will be sent for publication after review by the Medical Research center. We also plan to present the results of the study in various international conferences.

References

1. Cunningham, F. G., Leveno, K. J., Bloom, S. L., Spong, C. Y., Dashe, J. S., Hoffman, B. L., & Casey, B. M. (2018). Williams Obstetrics, Twenty-Fifth Edition. McGraw-Hill Education.

2. Mustoe, T. A., Cooter, R. D., Gold, M. H., Hobbs, F. D., Ramelet, A. A., Shakespeare, P. G., & Ziegler, U. E. (2002). International clinical recommendations on scar management. Plastic and reconstructive surgery, 110(2), 560-571.

3. Mustoe, T. A. (2008). Evolution of silicone therapy and mechanism of action in scar management. Aesthetic Plastic Surgery, 32(1), 82-92.

4. Juckett, G., & Hartman-Adams, H. (2009). Management of keloids and hypertrophic scars. American Family Physician, 80(3), 253-260.

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5. Gold, M. H., Berman, B., Clementoni, M. T., Gauglitz, G. G., Nahai, F., Murcia, C., ... & Solish, N. (2014). Updated international clinical recommendations onscar management: part 2—algorithms for scar prevention and treatment. Dermatologic Surgery, 40(8), 825-831.

6. Sidgwick, G. P., McGeorge, D., & Bayat, A. (2015). A comprehensiveevidence-based review on the role of topicals and dressings in the managementof skin scarring. Archives of Dermatological Research, 307(6), 461-477.

7. Winter, G. D. (1962). Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. Nature, 193(4812), 293-294.

8. Mustoe, T. A., Gurjala, A., The, M. H., Kirschner, R. E., Ragoowansi, R., Susarla, S., ... & Stotland, M. A. (2009). Dermal tissue regeneration by a small peptide occurring in high yield in Xenopus laevis. Journal of Plastic, Reconstructive & Aesthetic Surgery, 62(12), 1746-1752.

Appendices

Data collection sheet Questionnere/Survey and Research consent form.

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