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Comparision of oestrogen cream and aqueous cream in the management of ulcers caused by pelvic organ prolapse

Submission date
02/04/2021

Recruitment status
No longer recruiting

Registration date
08/04/2021

Overall study status
Completed

Last Edited
04/05/2021

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Pelvic organ prolapse is when 1 or more of the organs in the pelvis slip down from their normal position and bulge into the vagina. It can be the womb (uterus), bowel, bladder or top of the vagina. A prolapse is not life-threatening, but it can cause pain and discomfort.
This study is conducted to compare oestrogen cream aqueous cream soaked vaginal packing in the management of ulcers caused by pelvic organ prolapse and its effect on uterine safety. This study is important to show that the use of oestrogen cream in vaginal packing will result in faster ulcer healing compared to aqueous cream, and not cause adverse effects to the uterus and cervical lining.

Who can participate?
If you are suffering from decubitus cervical or vaginal ulceration(s) due to pelvic organ prolapse and do not have a history or presence of oestrogen-receptor positive cancer, unresolved pervaginal bleeding or premalignant and malignant lesion on the lower genital tract, you are eligible to participate in this study.

What does the study involve?
Once you are recruited and consented to the study, a vaginal pack with either oestrogen or aqueous cream will be done. Vaginal packing will be done twice a week in normal circumstances. You will be assessed during the follow up on whether repacking is necessary. At the 1st visit, you will be asked to answer the Prolapsed quality of life (P-QoL) Questionnaire and rate the pain of the uterovaginal prolapse at rest prior, during and after the packing. If the vaginal pack dislodge within 2days of packing, you will be asked to come back to Daycare during office hours for repacking. However, if the pack dislodge after 2 days, you will be asked to return to Daycare as scheduled for assessment and repacking if indicated.
At visit 2 and subsequent visit, vaginal packing will be removed and reassessed. If the ulcer is not healed, vaginal packing will be done. You will then be asked to rate the pain prior to and during the removal of gauze, and pain after the repacking if there should be one. You will also be asked to rate the odour/smell during the duration of packing in situ.
Once the ulcer is healed, a transvaginal ultrasound will be done to assess the endometrial

thickness, a pipelle sampling will be taken and a ring pessary will then be inserted until the operation date (for participants who are keen and fit for op) or until the follow-up date general gynaecology clinic.

What are the possible benefits and risks of participating?
By participating in this study, you may experience faster healing of decubitus ulcer and hence, avoid the delay in operation date.

Where is the study run from?
Department of Obstetrics and Gynaecology, University Malaya Medical Center (Malaysia)

When is the study starting and how long is it expected to run for?
February 2021 to December 2022

Who is funding the study?
Department of Obstetrics and Gynaecology, University Malaya Medical Center (Malaysia)

Who is the main contact?
Dr Chew Shir Lynn, shirlynn_chew85@yahoo.com

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NMRR-21-506-58628

Study information

Scientific Title
Randomised controlled trial: oestrogen vaginal packing effect on decubitus ulcer in pelvic organ prolapse

Study objectives

The use of oestrogen cream in vaginal packing of POP with decubitus ulceration compared to aqueous cream will result in faster ulcer healing and is safe.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/03/2021, University of Malaya Research Ethics Committee (Level 7, Research Management & Innovation Complex, University of Malaya, 50603 Kuala Lumpur; +603-79674525; pen_ippp@um.edu.my), ref:NMRR-21-506-58628

Study design
Single center intervention double-blinded randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Treatment of decubitus ulcers in pelvic organ prolapse

Interventions
Recruitment:
Women with POP and decubitus ulcer presented to the gynaecology clinic.
A Patient Information Sheet with essential information on the trial will be provided to all potential participants. The recruiter will also provide any other information sought, emphasize the voluntary nature of participation, reinforce the point that care will not be affected if trial participation is declined and that the participant may withdraw from the study at any time without having to provide a reason and their subsequent care will not be affected in any way.
Written consent will be obtained from all who agreed to participate.
Relevant demographic, medical data and POP Symptom/QoL Questionnaire will be collected as per the Case Report Form.

Randomisation:
1. Participants will be randomized into 2 groups
a. Aqueous cream-soaked vaginal packing vs
b. Oestrogen soaked vaginal packing
2. Randomisation will be generated by random sequence generator, provided by random.org to avoid bias, and labelled on an opaque envelope, which will be taken out from a designated box upon recruitment of the patient, which will determine which arm the patient belongs to.

Double Blinding:
Investigator A will be assigned to perform the packing of trial participants, however, will not be involved in assessing for final ulcer healing or peri-surgical outcomes.
Investigators involved in assessing ulcer healing or performing the surgery are designated Investigator B.
Participants will not be told their allocated packing cream. A set volume of cream eg14g is expressed into containers marked A and B and kept in the fridge by Investigator A in batches as

the study progresses.
This randomization card will be replaced into a new opaque envelope with the corresponding trial number, sealed and kept in designated trial files to be reopened at her next visit. This step is repeated at each packing visit, including at the final visit when the ulcer has healed.

Packing [Visit 1]:
The ulcer(s) individual site shape, size and depth at recruitment will be recorded in the Ulcer Chart.POP will be reduced into the vagina and vaginal packing will be performed according to the standard practice of the unit using the allocated cream.
For participants who are randomized to cream B (Oestrogen-soaked vaginal packing), a roller gauze (measuring 5cm x 180cm) will be soaked in saline solution and wringed dry until no saline solution is dripping. It is then applied with 2g Premarin cream which is measured and withdrawn from the containers using the applicator provided.
Similarly, for participants who are randomized to cream A (Aqueous cream-soaked vaginal packing), a roller gauze (measuring 5cm x 180cm) will be soaked in saline solution and wringed dry until no saline solution is dripping. By using the same applicator from the Premarin packaging, the aqueous cream is withdrawn from the container up to the 2g marking and applied to the roller gauze.
A new dressing set and speculum will be used whenever there is an inspection or packing of vagina. Both gauzes will be prepared under clean environment after the inspection of the decubitus ulcer and inserted into the vagina until the introitus under aseptic technique.
The participant will be asked to answer the Prolapsed quality of life (P-QoL) Questionnaire and rate the pain of the pelvic organ prolapse at rest prior to the packing. After the packing, the participant will rate the pain associated with packing using a Visual Numerical Rating Scale (VNRS – scored 0 to 10) and rate their satisfaction in regards with the smell/odor after the procedure using Likert's scale.
Prior to discharge home, an appointment will be given within the week as per unit standard care protocol. Mobilisation and discharge home after packing as per standard protocol.

Inadvertent Pack Extrusion:
If the pack falls out before scheduled removal (within 2 days), it will be replaced by Investigator A following the procedures of opening the sealed numbered envelope, packing with the allocated cream. If repacking is performed by Investigator B as a last resort by Investigator A is unavailable, the infringement will be recorded.
If the pack falls out after 2 days, participants will be asked to come back on the scheduled visits. After repacking of an inadvertent pack extrusion, a follow up appointment should be rescheduled as per unit protocol which would be the official trial VISIT. [Record]

Subsequent Visit(s) [Record as Visit 2]
Unit protocol mandates a change in the vaginal pack twice a week in normal circumstances. Participants will be asked to rate the pain prior and during the removal of vaginal packing at every visit using the VNRS score.
Participants will also be asked to rate the ordor / smell during the duration of the packing by using the Likert's 5 point scale.
The pack will then be removed by Investigator A who will remove any residual cream prior to assessment of ulcer healing by Investigator B. Investigator B will then assess the ulcer(s) using the Ulcer Chart recording for each ulcer, its site, size, shape and depth. Pictures of the ulcer(s) will be taken, labelled and kept in the participant's folder. Investigator B will then be asked to rate the ordor / smell during the duration of the examination of the ulcer by using the Likert's scale.
Only at the first follow up visit (Visit 2) that Investigator B will be asked with a Tick Box Questionnaire (two-answer option only available Oestrogen or Aqueous Cream) what type of

cream has been used in the vaginal pack.
If ulcer(s) healing is incomplete, Investigator B will instruct Investigator A to repack according to participant's Randomisation Card.
Investigator A will open the sealed envelope, cross-check the participant's identity against the hospital sticker affixed to the back of the Randomisation Card and then repack with the allocated cream. After the repacking of the vagina, the participant will be asked to rate the pain during the repacking procedure using the VNRS score.
A follow up appointment will be made as per unit standard care protocol until the ulcer is healed.
If the ulcer(s) is healed, investigator B will indicate on Ulcer Chart: complete healing, and pictures will be taken, labelled and kept in the patient's folder.

"Final" Visit (Ulcer Healed)
When the ulcer is healed, Investigator B will indicate on Ulcer Chart: complete healing. Pictures of the healed ulcer(s) will be taken, labelled and kept in the participants folder.
The participant will be asked to provide a Satisfaction Score (VNRS 0 to 10) with the entire treatment process leading to ulcer healing
All participants will be scan for endometrium thickness using a transvaginal ultrasound scan and a pipelle sampling will be taken (earlier if indicated). Ring pessary will be offered to participants.

Surgery
Standard peri-operative procedure and care will apply to all participants who are keen and fit for surgery.
On the operating table prior to the start of surgery, Investigator B (the primary surgeon) will be asked to answer Tick Box Questionnaire (two-answer option only available Oestrogen or Aqueous Cream) what type of cream has been used in the vaginal packing.
At the end of surgery, Investigator B (the primary surgeon) will be asked to answer Tick Box Questionnaire (two-answer option only available Oestrogen or Aqueous Cream) what type of cream has been used in the vaginal packing.
The entire hysterectomy specimen is to be forwarded to a blinded histopathologist for standard assessment with standardized evaluation to detect endometrial/endocervical glandular hyperplasia or worse. (HPE Report 1)

The following peri-operative outcomes are also recorded onto the Case Report Form
- Surgeon's satisfaction toward the tissue's condition during operation (VNRS 0 to 10)
- Operating time (knife to skin to last closing suture)
- Per-operative blood loss
- Intraoperative complications (inadvertent injury to adjacent structures)
- Post-surgical resumption of urination
- Post-surgical hospital stay

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
oestrogen cream, aqueous cream

Primary outcome(s)

1. Time to complete healing of the decubitus ulcers. Decubitus ulcer(s) will be assessed by Investigator B at every visit. Complete healing is assessed by direct visualisation of the cervix and vagina
2. Presence of endometrial hyperplasia from histopathological examination of endometrial sampling/hysterectomy specimen. Histopathological examination of endometrium will be done at the time of ulcer healing by using a pipelle sampling or when the patient undergo hysterectomy

Key secondary outcome(s))
1. Pain is measured using the visual numerical rating score (VNRS) at 1st visit after the packing, and at subsequent visit, before and during the packing
2. Satisfaction of odour / smell is measured using Likert's scale at 1st visit after packing and at subsequent visit prior to packing and assessment
3. Overall satisfaction with the packing regimen is assessed using Visual Numerical Rating Score (VNRS) at the point of ulcer healing
4. Peri-surgical outcomes is assessed after operation using patient records:
4.1. Surgeon's satisfaction toward the tissue's condition is measured using Visual Numerical Rating Score
4.2. Duration of surgery
4.3. Peri-operative blood loss
4.4. Intraoperative complications (inadvertent injury to adjacent structures)
4.5. Post surgical resumption of urination
4.6. Duration of hospital stay

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Pelvic organ prolapse with decubitus ulcer
2. One or more decubitus ulcer present on vaginal or cervical epithelium at 1cm or more.
3. Intact uterus with endometrium thickness of no more than 4 mm
4. Planned treatment with vaginal packing
5. Mental competency to provide consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria

1. History or presence of oestrogen-receptor positive cancer
2. Unresolved suspicion of endometrial or glandular endocervical pathology
3. Premalignant and malignant lesion on the lower genital tract

Date of first enrolment
12/04/2021

Date of final enrolment
30/04/2022

Locations

Countries of recruitment
Malaysia

Study participating centre
University Malaya Medical Center
Kuala Lumpur
Malaysia
59100

Sponsor information

Organisation
University Malaya Medical Centre

ROR
https://ror.org/00vkrxq08

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Malaya Medical Centre

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			04/05/2021	No	No