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Carrageenan Against Transmission of Cervical Human papillomavirus (HPV)

Submission date
10/02/2012

Recruitment status
No longer recruiting

Registration date
07/03/2012

Overall study status
Completed

Last Edited
04/07/2023

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[X] Individual participant data

Plain English summary of protocol

Background and study aims
Worldwide, cervical cancer is the second leading cause of cancer in women. Cervical cancer is most common in Latin America, eastern and southern Africa, and the Caribbean. Because it is much more common in developing countries, it has been described as a disease of poorer nations. We now know that human papillomavirus (HPV) is the central cause of cervical cancer. HPV is the most common sexually transmitted infection, and most sexually active women acquire HPV infection over their lifetime. Usually these infections are not noticed or only cause external warts, which although benign, are difficult to treat and often lead to social stigmatization. Most HPV infections will not lead to cervical cancer, only those that involve certain types of this virus and that persist for a long time. There is currently a vaccine available that prevents the types of HPV infection that cause most cases of cervical cancer, but unfortunately it is effective only before and not after the infection is established. Furthermore, HPV vaccination is too expensive for use in developing countries. An HPV inhibitory compound in the form of a topical microbicide that kills viruses might be useful for blocking the spread of HPV. Researchers have identified carrageenan (an inexpensive gelling agent) as a potent HPV infection inhibitor. There has been interest in carrageenan as a topical microbicide targeting HIV and herpes viruses, but laboratory tests have found that it is a thousand times more effective against HPV. If an inexpensive topical microbicide is identified that prevents HPV, this would serve as a very useful method to help reduce the burden of HPV infection and cervical cancer in developing and developed countries, in a cost-effective way. The main aims of this study are to find out whether a topical microbicide that contains carrageenan is effective in preventing new HPV infections and clearing existing HPV infections.

Who can participate?
We will recruit female students aged 18 or older and living in Montreal. Eligible subjects must: plan to remain in Montreal for at least the next year; have had vaginal sex with a male partner during the last 3 months and expect that they will do so again in the next 3 months; understand French or English; be willing to comply with follow-up for at least 12 months; have an intact uterus; have no history of cervical lesions/cancer or genital warts; not be pregnant or planning to immediately become pregnant and not currently breast-feeding; not had a recent (within the last 6 weeks) pregnancy, abortion, or genital surgery; be using a medically acceptable method of contraception and intend to use it for the duration of the trial; have no HIV infection; have no

known allergy or hypersensitivity to vaginal lubricants; and have no known allergy to all of the ingredients of the study product or placebo. Since there are many HPV types, this trial will not exclude women who have a detectable HPV type upon enrolment as these women could still become infected with another HPV type. The McGill and Concordia University Health Services Clinics and the CISSS (Centre intégré de santé et de services sociaux) de la Montérégie-Centre will serve as recruitment centers. The clinics provide medical care year-round to full-time students. Recruitment will be bolstered through campus-wide appeals (e.g. posted notices, e-mails to student lists). Additional efforts will include mail-outs to students living in residence, presentations to students in professional schools (e.g. medical school), and information booths at student activities. To enrol, participants will have to give their informed consent.

What does the study involve?
Two different lubricant gels are being compared in this trial, i.e., one that contains carrageenan (treatment) and one that does not (placebo/dummy). Participants will be asked to apply the gel that they receive to their genital area and inside their vagina prior to vaginal sex. They will also be asked to use the gel every other day during the first month, regardless of whether or not they have sex. Over the course of the study, participants will be asked to complete questionnaires and to provide cervical samples for HPV testing. While one group will receive the lubricant that contains carrageenan, the other group will receive a lubricant that is similar but that does not contain carrageenan. Both groups will receive the exact same care throughout their involvement in the study.

What are the possible benefits and risks of participating?
The risks in this study are minimal as the collection of a vaginal specimen for HPV testing is a safe procedure. There is the possibility that slight discomfort might be felt during the insertion of the sampler to collect the specimen. Also, using either carrageenan or the comparison gel may cause itching, burning or pain but these symptoms are unlikely (<5% chance). These gels are readily available in drug stores and cosmetic shops as sexual lubricants. Taking part in this study may or may not make participants health better. While we hope that the intervention under study will be useful in protecting against infection with HPV, there is no proof of this yet.

Where is the study run from?
The McGill and Concordia University Health Services Clinics and the CISSS (Centre intégré de santé et de services sociaux) de la Montérégie-Centre will serve as recruitment centers. Study oversight and data management will be carried out at McGill Universitys Division of Cancer Epidemiology.

When is the study starting and how long is it expected to run for?
Patients will be enrolled in the study between April 2012 and July 2015, or until the required sample size has been reached. Follow-up examinations will continue until October 2021.

Who is funding the study?
Canadian Institutes of Health Research (CIHR) (Canada).

Who is the main contact?
Dr Eduardo Franco (Principal Investigator)
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Study information

Scientific Title
Randomized controlled trial evaluating the efficacy of carrageenan as a topical microbicide against HPV Infection

Acronym
CATCH

Study objectives
1. To evaluate the efficacy of carrageenan in reducing genital HPV incidence, i.e., in preventing new HPV infection, in young sexually active women.
2. To evaluate the efficacy of carrageenan in reducing genital HPV prevalence, i.e., in accelerating clearance of existing infections, in young sexually active women.
(added 14/10/2022)
3. To evaluate participant adherence as measured by behavioural characteristics assessed by questionnaires.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. The Institutional Review Board, McGill University, Canada, 13/12/2011, ref: A12-M93-09B
2. Health Canada - Natural Health Products Directorate, 18/07/2011, ref: 169160
3. The Human Research Ethics Committee Office of Research, Concordia University, 12/04/2012, ref: 10000599 – UH2012-036
4. The CISSS de la Montérégie-Centre, 11/02/2016, ref: AA-HCLM-15-040

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Human papillomavirus infection

Interventions
Current interventions as of 01/03/2017:
Intervention: Treatment with carrageenan-containing vaginal gel, self-applied every other day (whether or not participants have intercourse) for the first month and apply the gel prior to and following each act of vaginal or anal intercourse during the entire follow up period (1 year).

Control: Treatment with placebo vaginal gel, self-applied every other day (whether or not participants have intercourse) for the first month and prior to each act of vaginal or anal intercourse during the entire follow up period (1 year).

Prior to and following vaginal intercourse, participants will be asked to apply the study gel either directly inside their vagina and externally on the genitals. During intercourse, additional

lubricant can be applied as desired. During the first month, participants will be asked to apply the gel both inside their vagina, as well as on to their genitals every other regardless of whether or not they have intercourse. Study participants will be asked to continue using the assigned intervention for the complete follow up period (1 year) along with any other methods of contraception and/or sexually transmitted infection (STI) prevention (e.g., condoms).

Previous interventions:
Intervention: Treatment with carrageenan-containing vaginal gel, self-applied every other day (whether or not participants have intercourse) for the first month and prior to each act of vaginal or anal intercourse during the entire follow up period (1 year).

Control: Treatment with placebo vaginal gel, self-applied every other day (whether or not participants have intercourse) for the first month and prior to each act of vaginal or anal intercourse during the entire follow up period (1 year).

Prior to vaginal intercourse, participants will be asked to apply the study gel either directly inside their vagina and externally on the genitals. During intercourse, additional lubricant can be applied as desired. During the first month, participants will be asked to apply the gel both inside their vagina, as well as on to their genitals every other regardless of whether or not they have intercourse. Study participants will be asked to continue using the assigned intervention for the complete follow up period (1 year) along with any other methods of contraception and/or sexually transmitted infection (STI) prevention (e.g., condoms).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Carrageenan

Primary outcome(s)
1. Reduction in HPV incidence
2. Presence of:
2.1. A newly detected vaginal infection in someone who was HPV negative at enrolment or
2.2. HPV types other than those observed at enrolment
3. Clearance of infections with HPV types observed at baseline

HPV DNA detection and genotyping of vaginal samples will be done by the PGMY polymerase chain reaction protocol. HPV infection status will be measured at baseline (enrolment/time 0), 14 days and 1, 3, 6, 9 and 12 months after enrolment.

Key secondary outcome(s)
Current secondary outcome measures as of 14/10/2022:

Patient adherence to the intervention as measured by behavioural characteristics assessed by questionnaires.

Previous secondary outcome measures:

Reduction in HPV prevalence (i.e., clearance of infections with HPV types observed at baseline).

HPV DNA detection and genotyping of vaginal samples will be done by the PGMY polymerase chain reaction protocol. HPV infection status will be measured at baseline (enrolment/time 0), 14 days and 1, 3, 6, 9 and 12 months after enrolment.

Completion date
20/10/2021

Eligibility

Key inclusion criteria
Added 01/03/2017: Current inclusion criteria as of 17/11/2014:
1. Female aged 18 or older living in Montreal
2. Plan to remain in Montreal for at least the next year
3. Have had vaginal sex with a male partner during the last 3 months and expect that they will do so again in the next 3 months, regardless of whether or not the male partner(s) will change
4. Not currently in a relationship that has lasted longer than 6 months
5. Be willing to follow study instructions
6. Understand French or English
7. Be willing to comply with follow-up for at least 12 months
8. Have an intact uterus
9. Have no history of cervical lesions/cancer or genital warts
10. Not be pregnant or planning to immediately become pregnant and not currently breastfeeding
11. Not had a recent (within the last 6 weeks) pregnancy, abortion, or genital surgery
12. Be using a medically acceptable method of contraception and intend to use it for the duration of the trial
13. Have no HIV infection
14. Have no known allergy or hypersensitivity to vaginal lubricants
15. Have no allergy to all of the ingredients of the study product or placebo

Previous inclusion criteria from 12/09/2013:
1. Female aged 18-29 living in Montreal
2. Plan to remain in Montreal for at least the next year
3. Have had vaginal sex with a male partner during the last 3 months and expect that they will do so again in the next 3 months, regardless of whether or not the male partner(s) will change
4. Not currently in a relationship that has lasted longer than 6 months
5. Be willing to follow study instructions
6. Understand French or English
7. Be willing to comply with follow-up for at least 12 months
8. Have an intact uterus
9. Have no history of cervical lesions/cancer or genital warts
10. Not be pregnant or planning to immediately become pregnant and not currently breast-feeding
11. Not had a recent (within the last 6 weeks) pregnancy, abortion, or genital surgery
12. Be using a medically acceptable method of contraception and intend to use it for the duration of the trial

13. Have no HIV infection
14. Have no known allergy or hypersensitivity to vaginal lubricants
15. Have no allergy to all of the ingredients of the study product or placebo

Original inclusion criteria:
1. Female aged 18-24 living in Montreal
2. Plan to remain in Montreal for at least the next year
3. Have had vaginal sex with a male partner during the last 30 days and expect that they will do so again in the next month, regardless of whether or not the male partner(s) will change
4. Not currently in a relationship that has lasted longer than 3 months
5. Be willing to follow study instructions
6. Understand French or English
7. Be willing to comply with follow-up for at least 12 months
8. Have an intact uterus
9. Have no history of cervical lesions/cancer or genital warts
10. Not previously vaccinated against HPV
11. Not be pregnant or planning to immediately become pregnant and not currently breast-feeding
12. Not had a recent (within the last 6 weeks) pregnancy, abortion, or genital surgery
13. Be using a medically acceptable method of contraception and intend to use it for the duration of the trial
14. Have no HIV infection
15. Have no known allergy or hypersensitivity to vaginal lubricants
16. Have no allergy to all of the ingredients of the study product or placebo

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Total final enrolment
461

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
15/04/2012

Date of final enrolment
30/09/2020

Locations

Countries of recruitment
Canada

Study participating centre
McGill University
Montreal
Canada
H4A 3T2

Study participating centre
CLSC Samuel-de-Champlain
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Sponsor information

Organisation
Canadian Institutes of Health Research (CIHR) (Canada)

ROR
https://ror.org/01gavpb45

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 27/03/2023:
The anonymized participant-level data, code, and codebook are publicly available on the McGill Dataverse under a CC-BY 4.0 License/Data Use Agreement (https://doi.org/10.5683/SP3/0DS6FP).

Previous IPD sharing statement:
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Eduardo Franco (eduardo.franco@mcgill.ca)

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		08/06/2023	04/07/2023	Yes	No
Protocol article		03/09/2021	07/09/2021	Yes	No
Basic results		02/03/2023	02/03/2023	No	No
Dataset		24/02/2023	27/03/2023	No	No
Interim results article	interim results	01/02/2019	23/10/2020	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes