ISRCTN15551486 https://doi.org/10.1186/ISRCTN15551486

Ibuprofen for menstrual cramps

Submission date	Recruitment status	[_] Prospectively registered
02/12/2024	Recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
17/04/2025	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
23/04/2025	Urological and Genital Diseases	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Up to 94% of adolescent girls and young women suffer from menstrual cramps (cramps, also called primary dysmenorrhea [PD]), out of which over 30% report moderate to severe pain and 20-30% increased school/work absenteeism and the potential development of chronic pain. Current guidelines recommend nonsteroidal anti-inflammatory drugs (NSAIDs) as the first-line treatment, with standard cramp therapy as 200-400 mg ibuprofen initially, then 200 mg every 4-8 hours. However, only half of women on ibuprofen for cramps report sufficient or effective pain relief. This may be explained by the current regimen failing to take into account Ibuprofen's short half-life of 1.6-2 hours and its need to work "upstream" (via blocking prostaglandin synthesis). Despite extensive clinical and instructional experience (https://www.cemcor.ca/resources/painful-periods), a more frequent dosing regimen that better aligns with drug characteristics has never previously been tested.
This study aims to test an intense (as-soon-as-cramps-start-to-return) ibuprofen dosing regimen vs a standard-of-care regimen for the treatment of menstrual cramps to answer whether women will perceive compared to their last 3-months' experience that intense ibuprofen dosing significantly decreases menstrual cramp intensity during 1 week of documented therapy compared with standard-of-care Ibuprofen dosing.

Who can participate?
Menstruating individuals 16-25 years of age in Metro Vancouver with regular menstrual cycles, about 1 month apart, who experience moderate to severe cramps interfering with daily life and activities.

What does the study involve?
Participants are randomly allocated to one of two groups to receive intensive or standard ibuprofen dosing for the treatment of menstrual cramps (primary dysmenorrhea). The experimental and control groups will receive corresponding instructions on when and how to take ibuprofen, as well as to record parameters in their menstrual cycle diary and the ibuprofen use recording form. The study duration per participant will be up to 16 days, with 1 day of screening and enrolment, 7 premenstrual days and 7 menstrual cycle days for independent data collection, and 1-2 days for follow-up and completing a final questionnaire.

What are the possible benefits and risks of participating?
Participants will benefit from receiving Ibuprofen tablets prescribed for the treatment of their

moderate to severe menstrual cramps (a total of 90 200 mg tablets), menstrual cups (if requested, with counseling on how to use one), and education and skills to improve personal health monitoring.
Risks include adverse effects from taking ibuprofen, which will be minimized through eligibility screening and appropriate patient counseling.

Where is the study run from?
Centre for Menstrual Cycle and Ovulation Research (Canada)

When is the study starting and how long is it expected to run for?
April 2024 to December 2025

Who is funding the study?
1. Centre for Menstrual Cycle and Ovulation Research (Canada)
2. Pure Integrative Pharmacy (Canada)
3. UBC Faculty of Medicine (Canada)

Who is the main contact?
Dr Jerilynn C. Prior, jerilynn.prior@ubc.ca or dhani.kalidasan@ubc.ca

Study website
https://www.cemcor.ca/menstrual-cramps-ibuprofen-therapy-study

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Dr Jerilynn Prior

ORCID ID
http://orcid.org/0000-0003-3232-0597

Contact details
Centre for Menstrual Cycle and Ovulation Research (CeMCOR)
Division of Endocrinology, Faculty of Medicine, University of British Columbia
Room 4111 - 4th Floor, 2775 Laurel Street
Vancouver
Canada
V5Z 1M9
+1 (0)604 875 5927
jerilynn.prior@ubc.ca

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Treatment of menstrual cramps in young adult women— randomized controlled trial of standard versus experimental dosing of ibuprofen

Study objectives
It is hypothesized that the intense ibuprofen dosing (experimental arm) will decrease cramp intensity by 60% (Final Questionnaire recording of -3) versus 20% (-1) for the standard arm with both compared with cramps in the last three cycles.

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 12/11/2024, Clinical Research Ethics Board (CREB), University of British Columbia (UBC CREB Office: Room 210 - Research Pavilion 828 West 10th Avenue, Vancouver, V5Z 1M9, Canada; +1 (0)604 827 5310; pia.ganz@ubc.ca), ref: H24-03415

Study design
Single-centre open-label semi-blinded (statistician-blinded) randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
University/medical school/dental school

Study type(s)
Quality of life, Treatment, Safety, Efficacy

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Primary dysmenorrhea (menstrual cramps)

Interventions
Participants are randomized to intensive or standard ibuprofen dosing for the treatment of menstrual cramps (primary dysmenorrhea).

Experimental (intense ibuprofen dosing) - Their prescription will read “Following the initial 400 mg dose with food/milk, take another 200 mg tablet with food/milk as soon as cramps start to return, even if this is only 1-2 hours since the last dose, to a maximum of 12 tabs every 24 hours.”

Standard (recommended Ibuprofen for cramps dosing) – Their prescription will read “Following the initial 400 mg dose with food/milk, take another 200 mg tablet with food/milk every 4-6 hours to a maximum of 12 tabs every 24 hours.”

The study duration per participant will be up to 16 days, with 1 day of screening and enrolment, 7 premenstrual days and 7 menstrual cycle days for independent data collection, and 1-2 days for follow-up and completing a final questionnaire.

Intervention Type
Drug

Pharmaceutical study type(s)
Dose response

Phase
Not Applicable

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

Primary outcome measure
The perceived change (scored -5, 0, +5) in cramp intensity on intensive ibuprofen dosing (experimental) versus standard-of-care ibuprofen dosing both as compared with usual cramp experience in the last 3 months, as recorded in the Final Questionnaire at the end of each volunteer’s participation

Secondary outcome measures
1. Variables relevant to participants’ cramp experience: changes in feeling of self-worth, feeling of energy and outside stresses recorded before and during flow, as scored on a scale from 1-5, as recorded by a daily Menstrual Cycle Diary© (Daily Diary) throughout the 14 days of this study
2. Amount of flow as recorded on the Daily Diary by number of soaked tampons +/- pads (normal size-soaked/day), or by volume scoring if they are using a menstrual cup
3. Gastrointestinal ibuprofen adverse effects: heartburn, stomach pain, nausea, vomiting, as recorded on the daily Ibuprofen Therapy Recording form during cramps
4. General menstrual flow or cramps adverse effects (headache, tiredness, diarrhea, sleep problems) recorded on the Daily Diary and the Ibuprofen Therapy Recording form throughout the trial and during cramps, respectively
5. Total mg of ibuprofen/day taken for menstrual cramps recorded using the daily Ibuprofen Therapy Recording form over each of the 1st to 7th menstrual cycle days
6. Remaining ibuprofen pill counts by random assignment (returning them to the participant) at the end of each volunteer’s trial participation
7. Mean menstrual cramp intensity scored on a scale from 0-4, by the Daily Diary during the time of experiencing cramps
8. Mean menstrual cramp duration as recorded >0 in the Daily Diary during the time of experiencing cramps
9. Cramps Score = (total days with cramps X mean cramp intensity), by prospective daily Menstrual Cycle Diary© records during the time of experiencing cramps

10. Perceived change in the duration of cramps on the Final Questionnaire at each volunteer's end of participation
11. Perceived change in the impact of cramps on daily life as reported on the Final Questionnaire at each volunteer's end of participation

Overall study start date
29/04/2024

Completion date
31/12/2025

Eligibility

Key inclusion criteria
Resident within Metro Vancouver with access to offices in the Diamond Centre near Vancouver General Hospital
1. Menstruating individuals 16-25 years of age
2. Regular menstrual cycles, approximately 1 month apart (range 21-35 days or 3-5 weeks)
3. Moderate to severe cramps (problematic cramps) interfering with daily life and activities (as defined by the screening questionnaire)
4. If sexually active with a man, may be using non-hormonal contraceptives (condoms, diaphragm either or both with vaginal spermicide, or the copper IUD)

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
16 Years

Upper age limit
25 Years

Sex
Female

Target number of participants
66

Key exclusion criteria
1. Hormonal contraceptives (including combined hormonal contraceptives, levonorgestrel-releasing IUDs*, hormonal implant, Depo-Provera, progestin-only pill) and emergency contraceptives within the last cycle, or any reproductive hormone use within the last 3 months.
2. Have inability to take or should not take Ibuprofen as described by the screening questionnaire. For example, a hypersensitivity to Ibuprofen or other NSAIDs or any ingredients in the formulation of the Ibuprofen tablets, which may include microcrystalline cellulose, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide, hydroxypropyl cellulose, polyethylene glycol, titanium dioxide, D&C yellow #10 and FD&C yellow #6, carnauba wax.

3. Have complete or partial syndrome of acetylsalicylic acid (ASA) intolerance (rhinosinusitis, urticaria/angioedema, nasal polyps, asthma) in whom asthma, anaphylaxis, urticaria /angioedema, rhinitis or other allergic manifestations are precipitated by ASA or other NSAIDs, as per the contraindications section in the manufacturer product monograph.
4. Active gastric or duodenal ulcer, a history of recurrent ulceration, gastrointestinal bleeding, or active inflammatory disease of the gastrointestinal system. Patients with gastroesophageal reflux disease (GERD) are not excluded by these criteria.
5. Significant hepatic impairment or active liver disease.
6. History of severe kidney disease defined as eGFR <30ml/min.
7. Have suffered from an acute kidney injury (serum creatinine rise of 26 uM) in the past 6 weeks due to significant fluid loss.
8. Have systemic lupus erythematosus, as anaphylaxis-type reactions with fever have been documented to occur when Ibuprofen has been administered previously, as per the contraindication's sections in the manufacturer product monograph.
9. Endometriosis (by history, imaging or surgery).
10. Pregnant or postpartum for less than 6 weeks.
*Note: If we run into difficulty recruiting enough participants, we will consider including individuals with regular cycles (i.e., approximately 1 month apart) over the last 3 months, who have worn Kyleena for 60 days or Mirena for 5 years.

Date of first enrolment
01/04/2025

Date of final enrolment
30/11/2025

Locations

Countries of recruitment
Canada

Study participating centre
Centre for Menstrual Cycle and Ovulation Research
The Gordon and Leslie Diamond Health Care Centre
Room 4111 - 4th Floor, 2775 Laurel Street
Vancouver
Canada
V5Z 1M9

Sponsor information

Organisation
Centre for Menstrual Cycle and Ovulation Research

Sponsor details

Room 4111 - 4th Floor
2775 Laurel Street
Vancouver
Canada
V5Z 1M9
+1 (0)604 875 5927
cycles.cemcor@ubc.ca

Sponsor type
University/education

Website
https://www.cemcor.ubc.ca

Funder(s)

Funder type
University/education

Funder Name
Centre for Menstrual Cycle and Ovulation Research

Funder Name
University of British Columbia

Funder Name
Pure Integrative Pharmacy

Results and Publications

Publication and dissemination plan
Planned publication in Canadian Medical Association Journal (open access)

Intention to publish date
01/03/2026

Individual participant data (IPD) sharing plan
Each participant will learn which arm she was in and will know her results. The researchers will share the results of the whole study with participants through a password-protected site on the CeMCOR website. This will be created as soon as the results have been tabulated.

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?
Participant information sheet	version 2	01/04/2025	16/04/2025	No	Yes
Protocol file		24/03/2025	16/04/2025	No	No