STUDY PROTOCOL

Study Title: Effect of High Intensity Aerobic Exercise on Pain Threshold and Blood Pressure in Females with Primary Dysmenorrhea

Document Type: Study Protocol

Version: 1.0

Date of study: 5/9/24- 4/9/25

Principal Investigator: Swapneela Jacob

Institution: Lincoln University College, Selangor Malaysia

Department: Health Science

Clinical Trial Registration Number: Not yet assigned

Background

Primary Dysmenorrhea is the normal natural pain during menstruation without any underlying cause and pathological issue. It is a common condition in females of all ages. Pain threshold is overall reduced during the menstrual phase in females, and this leads to increased pain sensitivity in the body. Women percept pain from other body areas like neck, back, any injury pain during menstruation. This affects overall quality of life and participation in day-to-day activities. Blood pressure changes are seen during menstrual cycle and its variability in related to hypertension later in life. It is crucial to predict these changes earlier to prevent cardiovascular issues as ageing catches up in females more when they are menstruating. High intensity aerobic exercise is known to be a non-pharmacological method to improve the pain threshold and reduce pain perception and regulate blood pressure. The study explores the effect of high intensity aerobic exercise on pain threshold and blood pressure in females suffering from primary dysmenorrhea.

Study Type

Randomised Control Trial. The participants were randomly assigned into Experimental group that received High Intensity Aerobic Exercise and a Control group that received no treatment.

Study Setting

The study is conducted among the unmarried females from Universiti Tunku Abdul Rahman that includes students and staffs from all programs like Physiotherapy, Nursing, MBBS, Traditional Chinese medicine. The participants were female lecturers, admin staff working in the university. The study is carried out in the physiotherapy department of Universiti Tunku Abdul Rahman for performing the screening process for primary dysmenorrhea and also recording the pre-test and post- tests the outcome measurements exercise area was used to give high intensity aerobic exercise intervention to the participants.

Study population

The unmarried nulliparous female participants from the Universiti Tunku Abdul Rahman between the age 17-49 years were recruited for the study. The females were students from various courses in the MK faculty of medicine and health science Physiotherapy, MBBS, Nursing and Traditional Chinese Medicine) as well as the females working in the university as lecturers, admin and support staff.

Sampling Technique

Random sampling technique was used in the study. The screened and eligible participants were assigned to either Experimental or the Control group using online random

number generator tool. Online Research randomizer tool was used to divide the participants into either of the groups. Each participant was assigned a unique number to be used during the entire study. The study is a single blinded study. The Participants were unaware to which group they were assigned. Further instructions about the groups were given accordingly in a briefing during the first appointment. Research assistant was recruited and trained to assist in carrying out measurements of blood pressure and pain perception in both the groups and also to give instructions to the control group participants as well.

Research questions

1. What is the effect of High Intensity Aerobic Exercise on Pain Threshold and Blood Pressure in females with Primary Dysmenorrhea?
2. What is the effect of High Intensity Aerobic Exercise on Pain Threshold between Pretest and Posttest in the Experimental group?
3. What is the effect of High Intensity Aerobic Exercise on Pain Threshold between Pretest and Posttest in the Control group?
4. What is the effect of High Intensity Aerobic Exercise on Blood Pressure between Pretest and Posttest in the Experimental group?
5. What is the effect of High Intensity Aerobic Exercise on Blood Pressure between Pretest and Posttest in the Control group?
6. What is the effect of High Intensity Aerobic Exercise on Pain Threshold between the Experimental and Control group.
7. What is the effect of High Intensity Aerobic Exercise on Blood Pressure between the Experimental and Control group.

Research hypothesis

Hypothesis -There is a significant effect of high intensity aerobic exercise on pain threshold and blood pressure in females with primary dysmenorrhea between experimental and control group.

Null Hypothesis- These is no significant effect of high intensity aerobic exercise on pain threshold and blood pressure in females with primary dysmenorrhea between experimental and control group

Study procedure

-Participants will first undergo Primary Dysmenorrhea Screening to get diagnosed with Primary Dysmenorrhea. Once screened and diagnosed will be eligible to part of further study.

-Experimental group participants will under one week of accommodation exercise program to get used to high intensity exercises.

-Experimental and Control Group participants come to Physiotherapy department for **Pre-Test-** during day, day2, day3, day3 of menstruation and outcomes of Pain threshold and Blood Pressure will be measured and recorded.

- Experimental group participants will the come for High Intensity Aerobic Exercise Intervention three time a week/25 minute per session for coming four weeks and once they get the periods at the end of four weeks, during periods day1, day2, day 3, day4 pain threshold and blood pressure will be recorded. This is **Post Test 1**. The Control group participants will not come for any intervention and they will carry on with their normal lifestyle. They will come for Pain threshold and Blood pressure measurement at the end of 4^{th} week once their period comes.

-Experimental group will continue High Intensity Exercise Intervention for next four weeks again three time a week 25 minute/session and once they get the periods at the end of eight weeks, during periods day1, day2, day 3, day4 pain threshold and blood pressure will be recorded. This is **Post Test 2**. The Control group participants will not come for any intervention and they will carry on with their normal lifestyle. They will come for Pain threshold and Blood pressure measurement at the end of 8^{th} week once their period comes.

Safety monitoring

Adverse-event reporting and participant protection

A gynecologist conducted Primary Dysmenorrhea screening that included taking a detailed Menstrual History and Physical examination with abdominal and pelvis palpation. The Gynecologist Doctor was available if case of any emergency. After exercise session, electrolyte

drink was given to all participants. The participants were briefed and instructed to report any dizziness, or discomfort felt during or after the intervention.

Ethics

The Ethical Approval for the study was obtained from the UTAR Scientific and Ethical Review Committee (SERC) Universiti Tunku Abdul Rahman.

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STATISTICAL ANALYSIS PLAN (SAP)

Study Title: Effect of High Intensity Aerobic Exercise on Pain Threshold and Blood Pressure in Females with Primary Dysmenorrhea

Document Type: Statistical Analysis Plan (SAP)

Version: 1.0

Date of study: 5/9/24- 4/9/25

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Department: Health Science

Clinical Trial Registration Number: Not yet assigned

Analysis population

- Primary analysis population: ITT as participants were randomly allocated to intervention and control groups.

Sampling size

The sample size is calculated by using the G*Power program (F test) to calculate the sample size based on power analysis. Effect size 0.8, difference between two independent means A total of 110 participants will be needed for the study considering the 10% dropout rate. 55 in experimental group and 55 in the control group.

Statistical Method

Data was analyzed using Statistical Package for Social Sciences version 27 (SPSS Inc, Chicago, IL, USA). Descriptive analysis using frequency and percentages was used to summarize categorical data. Mean (M) and Standard Deviation (SD) were used to summarize continuous variables. Inferential analysis was carried out using Generalized Linear Mixed Model (GLMM). GLMM has the ability to model non- normal physiological data while simultaneously accounting for individual participant variability ensures that the observed improvements in pain thresholds and cardiovascular stability (SBP and DBP) are statistically valid and highly reliable. GLMM models each participant's unique baseline as a random intercept, allowing the model to isolate the true effect of the exercise intervention from the "noise" of individual biological differences. GLMM provides more clinically significant estimates as it accounts for both Fixed (Group, Time and Group*Time) and Random effects (Subject level variations).

This results in more precise estimates of the treatment effect. GLMM uses Maximum Likelihood Estimation (MLE) to fit the data, making it naturally more resistant to Type I errors (false positives) in repeated measures designs where time points are closely correlated. GLMM provides sophisticated fit indices, such as the Akaike Corrected Information Criterion (AICC) and the Bayesian Information Criterion (BIC) which allow to statistically prove that the chosen model (Gamma/Log) is the most efficient and accurate representation of the observed biological phenomena. The level of significance was set at 0.05 and 95% of confidence interval.

Normality testing- All the dependent variables tested for normal distribution assumption were found to not have normal distribution. This was also confirmed by the Kolmogorov-Smirnov test which showed $p < .001$ for each of the dependent variables.

Study objectives

Objectives

To find the effect of High Intensity Aerobic Exercise on pain threshold and blood pressure in females with primary dysmenorrhea.

General objective

To find the effect of High Intensity Aerobic Exercise on Pain Threshold and Blood Pressure in females with Primary Dysmenorrhea.

Specific objectives

1. To find the effect of High Intensity Aerobic Exercise on Pain Threshold between Pretest and Posttest in the Experimental group.
2. To find the effect of High Intensity Aerobic Exercise on Pain Threshold between Pretest and Posttest in the Control group.
3. To find the effect of High Intensity Aerobic Exercise on Blood Pressure between Pretest and Posttest in the Experimental group.
4. To find the effect of High Intensity Aerobic Exercise on Blood Pressure between Pretest and Posttest in the Control group.
5. To find the effect of High Intensity Aerobic Exercise on Pain Threshold between the Experimental and Control group.
6. To find the effect of High Intensity Aerobic Exercise on Blood Pressure between the Experimental and Control group.

Handling of missing data

Missing data was be assessed for the pain threshold and blood pressure outcomes in each study group. The number and percentage of missing observations, together with the reasons for missingness where available, were documented. Participants who discontinue the intervention remain in their originally allocated groups. The completeness of the collected data was be assessed before statistical analysis. All participants with available outcome measurements were

accounted in the analysis, and the completeness of the pain threshold and blood pressure measurements were verified.

Software

Data was analyzed using Statistical Package for Social Sciences version 27 (SPSS Inc, Chicago, IL, USA)

INFORM CONSENT (IF)

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(PARTICIPATION IN THIS RESEARCH IS VOLUNTARY)

1. Investigator's Name	:	Swapneela Jacob	**Faculty** :	FMHS PS
Title of research project	:	Effect of High Intensity Aerobic Exercise on Pain Threshold and Blood Pressure in Females with Primary Dysmenorrhea		
Purpose of study	:	The study aims to determine whether high-intensity aerobic exercise can affect pain threshold level and influence systolic and diastolic blood pressure in females experiencing primary dysmenorrhea.		
Procedure	:	Randomised Control Trial		
Risk and Discomfort	:	Fatigue/Delayed Onset muscle Soreness after exercise intervention		
Benefit	:	Electrolyte drink to participants after intervention Sports towel all participants after completion of study		
Payment	:	None		
Alternatives	:	NA		
Contact Person	:	Swapneela Jacob Principal Investigator-0172277671		

Note: 1. All volunteers involved in this study will not be covered by insurance
2. Contact person must be the principal investigator

2. Particulars of Volunteer (Volunteer Identifier/Label)
(Please use separate form if more than one volunteer)

Full Name	:			
Chinese character *(if applicable)*	:			
Date of Birth	:		Age :	
New Identity Card No.	:		Gender :	
Ethnic	:			
Blood Type	:			

Correspondence Address	:		
Telephone	:	Fax	:
Email	:		

3. Medical History

A brief medical history will be taken as detailed in **Appendix A**

4. Voluntary participation

You understand that participation in this study is voluntary and that if you decide not to participate, you will experience no penalty or loss of benefits to which you would otherwise be entitled. If you decide to participate, you may subsequently change your mind about being in the study, and may stop participating at any time. You understand that you must inform the principal investigator of your decision immediately.

5. Available Medical Treatment

If you are injured during your participation or in the course of the study or whether or not as a direct result of this study, UTAR will not be liable for any loss or damage or compensation or absorb the costs of medical treatment. However, assistance will be provided to you in obtaining emergency medical treatment.

6. Confidentiality

All information, samples and specimens you have supplied will be kept confidential by the principal investigator and the research team and will not be made available to the public unless disclosure is required by law.

7. Disclosure

Data, samples and specimens obtained from this study will not identify you individually. The data, samples and specimens may be given to the sponsor and/or regulatory authorities and may be published or be reused for research purposes not detailed within this consent form. However, your identity will not be disclosed. The original records will be reviewed by the principal investigator and the research team, the UTAR Scientific and Ethical Review Committee, the sponsor and regulatory authorities for the purpose of verifying research procedures and/or data.

By signing this consent form, you authorize the record review, publication and re-utilisation of data, information and sample storage and data transfer as described above

8. Declaration

I have read or have the information above read to me, in the language understandable to me. The above content has been fully explained to me.

I have asked all questions that I need to know about the study and this form. All my questions have been answered. I have read, or have had read to me, all pages of this consent form and the risks described. I voluntarily consent and offer to take part in this study. By signing this consent form, I certify that all information I have given, including my medical history, is true and correct to the best of my knowledge. **I will not hold UTAR or the research team responsible for any consequences and/or liability whatsoever arising from my participation in this study.**

9. Consent

If you wish to participate in this study, please sign below.

_____ _____

Signature of Volunteer IC. No.

_____ _____

Name of Volunteer Date

_____ _____

Signature of witness IC. No.

_____ _____

Name of witness Date

10. Statement of Principal Investigator

I have fully explained to the volunteer taking part in this study what he / she can expect by virtue of his / her participation. The volunteer who is giving consent to take part in this study

- Understands the language that I have used.
- Reads well enough to understand this form, or is able to hear and understand the contents of the form when read to him or her.
- Is of the age of majority of 18 or above.

To the best of my knowledge, when the volunteer signed this form, he or she understands:

- That taking part in the study is voluntary.
- What the study is about.
- What needs to be done.
- What are the potential benefits.
- What are the known risks.

A copy of this consent form has been given to the volunteer.

_____ _____

Name of Principal Investigator IC. No.

_____ _____

Signature of Principal Investigator Date

Note: *1. The principal investigator conducting the informed consent process, must sign* ***and*** *date form* ***at the same time as the volunteer****.*

Appendix A

Project Title :	Application No. *(As provided by* UTAR*)*	
	Volunteer Identifier / Label	

Medical History of Volunteer			
Have you ever had any of the following:		**Yes**	**No**
a	a serious illness or accident?		
b	an operation/ investigative procedure?		
c	yellow jaundice or hepatitis?		
d	tuberculosis?		
e	malaria?		
f	a tattoo?		
g	a blood transfusion?		
h	contact with any infectious disease?		
i	heart disease?		
j	high blood pressure (>140/90 mmHg)?		
k	asthma?		
l	kidney disease?		
m	diabetes?		
n	a stomach ulcer?		
Do you or family have any of the following:			

o	Cancer?		
p	Is a HIV carrier?		
q	psychiatric disease/ mental problem?		

If **human tissues samples** collected (*please complete the following*)

Sample		**Sampling**			
Identification	Type	Date	Location	Process (*if applicable*)	
				Random	Others (*please specify*)

Signature of Principal Investigator

swapneela