COMPRESSION STOCKING AT LABOUR EPIDURAL ANALGESIA ON MATERNAL HYPOTENSION: A BLINDED RANDOMISED SHAM-CONTROLLED TRIAL

RESEARCH PROPOSAL

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2025

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CHAPTER 1 : INTRODUCTION

Lumbar epidural is the most effective form of pain relief in labor [1] [2]with around 30% of laboring women in the UK and 60% in the USA receiving epidural analgesia [2]. It is known to result in transient maternal hypotension particularly at initiation, which may progress to the level of necessitating fluid or vasopressor therapy but this is not clearly associated with any adverse outcomes.[3]

Despite its widespread use, neuraxial anaesthesia which including epidural analgesia often results in significant hypotension due to blockade of preganglionic sympathetic fibres causing arterial and venous dilation with peripheral blood pooling which is further exacerbated in the supine position by compression of the inferior vena cava from the gravid uterus leading to reduce venous return and cardiac output.[4] It is now well established that the primary mechanism of hypotension is a marked reduction in systemic vascular resistance due to dilation of arteriolar resistance vessels, with a compensatory rise in heart rate and cardiac output.[5]

A 2020 meta-analysis shows that fluid co-loading which is commonly used to prevent maternal hypotension on epidural labour analgesia should not be relied upon as the sole preventive strategy. [6] Therefore, simple and non-invasive adjuncts such as compression stockings is of increasing interest.

Compression stockings such as thromboembolic deterrent (TED) stockings can enhance venous return. The incidence of hypotension can be reduced by increasing lower limb venous return and improving preload has physiological basis but direct evidence in labouring women is limited [7, 8]. TED stockings are low-cost and easy to implement measure may offer an effective, minimal side-effect method to reduce maternal hypotension at epidural analgesia in labour.

In a non-randomised study published in 2017, compression stockings have shown the incidence of hypotension 15min after epidural analgesia was significantly lower than in the control group (3.23% versus 23.3%) [7]. In a conference abstract published in 2017 as well, comparing control, thrombo-embolic deterrent (TED) stockings, or sequential compression device (SCD), hypotension occurred in 66.7% of patients in the control arm compared to 52.4% of patients in the TED arm, and 30.4% in the SCD arm (P=.038)[8]. Taken together,

these studies form a strong foundation for performing a double blind randomised controlled trial to explore TED stockings as a simple, effective intervention to reduce maternal hypotension after epidural analgesia in labour.

We hypothesize that fitted TED stockings applied before starting epidural analgesia in labour will lower maternal hypotension. We aim to evaluate the hypothesis in a double blind randomised controlled trial.

CHAPTER 2 : OBJECTIVE OF THE STUDY

To evaluate TED stockings in preventing maternal hypotension after epidural analgesia in labour

PRIMARY OUTCOMES

Maternal hypotension in the first 60 minutes after epidural analgesia (retrieved from electronic medical records after delivery)

Hypotension is defined as at least one occasion of:
i) >20% drop in systolic blood pressure,
ii) >20% drop in diastolic blood pressure
iii) >20% drop in mean arterial blood pressure
from baseline OR
iv) systolic blood pressure < 90mmHg

SECONDARY OUTCOMES

1. Maternal hypotension beyond 60 minutes of epidural up to delivery (retrieved from electronic medical records)

Hypotension is defined as at least one occasion of:
i) >20% drop in systolic blood pressure
ii) >20% drop in diastolic blood pressure
iii) >20% drop in mean arterial blood pressure
from baseline OR
iv) systolic blood pressure < 90 mmHg

2. Requirement for vasopressors and doses used, if any (retrieved from electronic medical records after delivery)
   a) within 60 minutes of epidural
   b) beyond 60 minutes of epidural up to delivery
3. Maternal symptoms (yes or no responses on direct questioning after 60 minutes of epidural)
   a. Nausea
   b. Dizziness
   c. Vomiting
   d. Palpitation
4. Fetal heart rate abnormality within 60 minutes of epidural (retrieved from electronic medical record)
   a) tachycardia (≥ 160 bpm for at least 15 minutes)
   b) fetal heart rate deceleration (15 bpm below baseline for at least 15 seconds on at **two** least occasions)
   c) fetal bradycardia (<100 bpm for at least 60 seconds)

d) clinical diagnosis of non-reassuring fetal status

5. Clinical diagnosis of non-reassuring fetal status up to delivery after delivery (retrieved from electronic records after delivery)
6. Epidural administration to delivery interval (retrieved from electronic records after delivery)
7. Estimated delivery blood loss (retrieved from electronic records after delivery)
8. Mode of Delivery (retrieved from electronic records after delivery)
   a. caesarean section
   b. instrumental delivery
   c. spontaneous vaginal delivery
9. Indication for operative delivery (retrieved from electronic medical records after delivery)
10. Patient satisfaction with the wearing of the compression stocking (assessment prior to discharge using 0-10 numerical rating scale)
11. Neonatal Outcomes
    a. APGAR scores at 1 and 5 minutes (retrieved from electronic medical records after delivery)
    b. Umbilical cord artery blood pH (retrieved from electronic medical records after delivery)
    c. Neonatal intensive care unit (NICU) admissions and indications (retrieved from electronic medical records after delivery)

CHAPTER 3 : METHODOLOGY

3.1 Study type and design

Interventional, single centre, double blind randomised controlled trial.

3.2 Study Area

University Malaya Medical Centre (UMMC)

3.3 Population of study

Term patients admitted for planned vaginal delivery who request or indicated for epidural analgesia

3.4 Sample size

During the conception phase of this trial, we performed a pre-study data collection exercise of a 100 women for 4 months duration who received epidural analgesia in labour. From the 100 cases, we found a 15% hypotension rate defined as >20% drop in SBP, DBP, MAP or SBP post <90mmHg (at least one of the four) in the first hour after epidural insertion.
Previous studies of lower limbs compression for epidural analgesia in labour have shown a reduction in maternal hypotension (3.23% versus 23.3%, adjusted odds ratio=0.1 [0.03; 0.35]) ([7] and [8]).
We assumed that TED stockings can reduce maternal hypotension by half reducing it from 15% to 7.5%.

Sample Size:X-Sectional, Cohort, & Randomized Clinical Trials

Two-sided significance level(1-alpha):	95
Power(1-beta, % chance of detecting):	80
Ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed with Outcome:	15
Percent of Exposed with Outcome:	7.5
Odds Ratio:	0.46
Risk/Prevalence Ratio:	0.5
Risk/Prevalence difference:	-7.5

	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size - Exposed	280	279	305
Sample Size-Nonexposed	280	279	305
Total sample size:	**560**	558	610

References

Kelsey et al., Methods in Observational Epidemiology 2nd Edition, Table 12-15
Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 &3.19
CC = continuity correction
Results are rounded up to the nearest integer.
Print from the browser menu or select, copy, and paste to other programs.

Results from OpenEpi, Version 3, open source calculator—SSCohort

The total sample size required is 560 with 280 in each arm.

3.5 Inclusion criteria

- Admitted for planned vaginal delivery
- Singleton pregnancies
- Term gestation (≥ 37 weeks)
- Compression stocking size ≤ 2XL
- Requesting or requiring epidural analgesia for labour pain management
- BP immediately before epidural ≥ 90/60 mmHg and considered suitable for epidural

3.6 Exclusion criteria

- Known severe hypertension in pregnancy (BP ≥ 160/110 mmHg)
- Known contraindications to epidural analgesia
- Cardiovascular conditions (e.g. arrhythmias, heart failure)
- Contraindications to compression stocking use (e.g. skin reaction, allergy to material, open wound, local infection)

3.7 Study flow / procedures

1) Patients admitted at term for planned vaginally delivery were screened for initial eligibility against study inclusion and exclusion criteria (Eligibility Assessment Form, EAF).

2) Patients meeting the initial criteria will be provided with the Patient Information Sheet (PIS), invited to ask questions and their queries responded to by the recruiting providers

3) Written informed consent is obtained from all participants.

4) Following consent, measurements of the thigh, calf, and leg length will be performed in the semi-recumbent position to establish correct stocking size as per standard protocol, and the measurements and matched stocking size were recorded.

5) Patients whose measurements are at the manufacturer's maximum size (3XL) are excluded at this stage as a larger sham size is not available to use

6) Investigators, not involved in recruitment, clinical care, or data collection will do:

a) The randomisation sequence is generated in random block of 4 or 8 with further randomisation within these blocks using online randomizer sealedenvelop.com
b) The allocation sequence is then sealed within individual numbered opaque envelope.
c) These envelopes are then assigned in strict sequence, the lowest numbered envelope still available to the newest recruit.
d) Unseal the numbered envelope allocated.
e) Check the intervention allocated (active intervention: correct size or control: 3 sizes larger or largest size available if 3 sizes larger is beyond 3XL) and obtain the stockings of the appropriate size as randomly allocated.
f) Packs the ‘size de-identified’ stockings into an identically numbered envelope (participant details affixed to outside) and seal the envelope.
g) If and when the final study criteria are fulfilled (labour epidural requested or indicated as per EAF), the numbered envelope with the participant details, and containing the allocated trial stockings will opened and the stockings within applied to the participant as per standard protocol.

7) Opening of the numbered envelope containing the trial stocking constitute the intention to treat.

8) The recruited and consented participant who did not fulfil final study criteria (EAF) is excluded and the prepared numbered envelope containing the trial stockings is not reused.

9) The allocated stockings will be applied within 30 minutes prior to the labour epidural.

10) Maternal blood pressure monitoring (systolic, diastolic, and MAP) will be performed via an automated upper-arm device:

a) Immediately before insertion of epidural catheter, to serve as the baseline blood pressure

b) Then as per our standard protocol after epidural administration

i) Every 5 minutes for the first 30 minutes

ii) Every 15 minutes for the next 30 minutes, and

iii) Every 30 minutes for the second hour

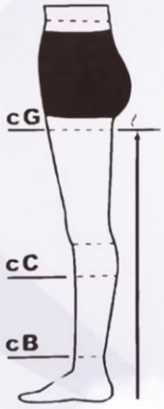
iv) Thereafter hourly if the trend is stable

11) Outcomes will be recorded as per the Case Report Form (CRF)

12) Compliance defined as the application of the allocated study stockings prior to epidural insertion and for at least one after will be recorded

Measurement Guide

Compression Stocking



Size	Circumference		
	cB	cC	cG
SS	17-20	26-32	38-47
S	20-23	30-36	44-55
M	23-26	34-40	50-61
L	26-29	38-44	56-68
XL	29-32	42-48	62-70
XXL	32-35	46-52	68-82
XXXL	35-38	50-56	74-88

Thigh high & Knee high

Wearing Methods

Trim Nails to Prevent Scratching Compression Socks

As shown,use both hands to turn the inside out except for the toes to heel area

Slightly open the pantyhose, start from the toe,and slowly put it to the heel

Slowly flipping the pantyhose, pull up & adjust to make the front of ankle smooth &wrinkle-free,and the toes are not too tight

After placing the socks over the ankles, in 'Z' shape to stretch the socks to the legs

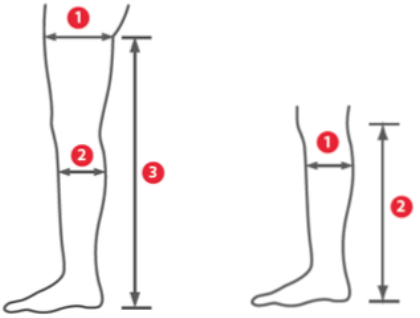
Continue to flip the inside of the pantyhose,while pulling up smoothly until to the thigh high

Procedure guideline:
Step-by-step guide to measuring and applying antiembolism stockings

Essential equipment:

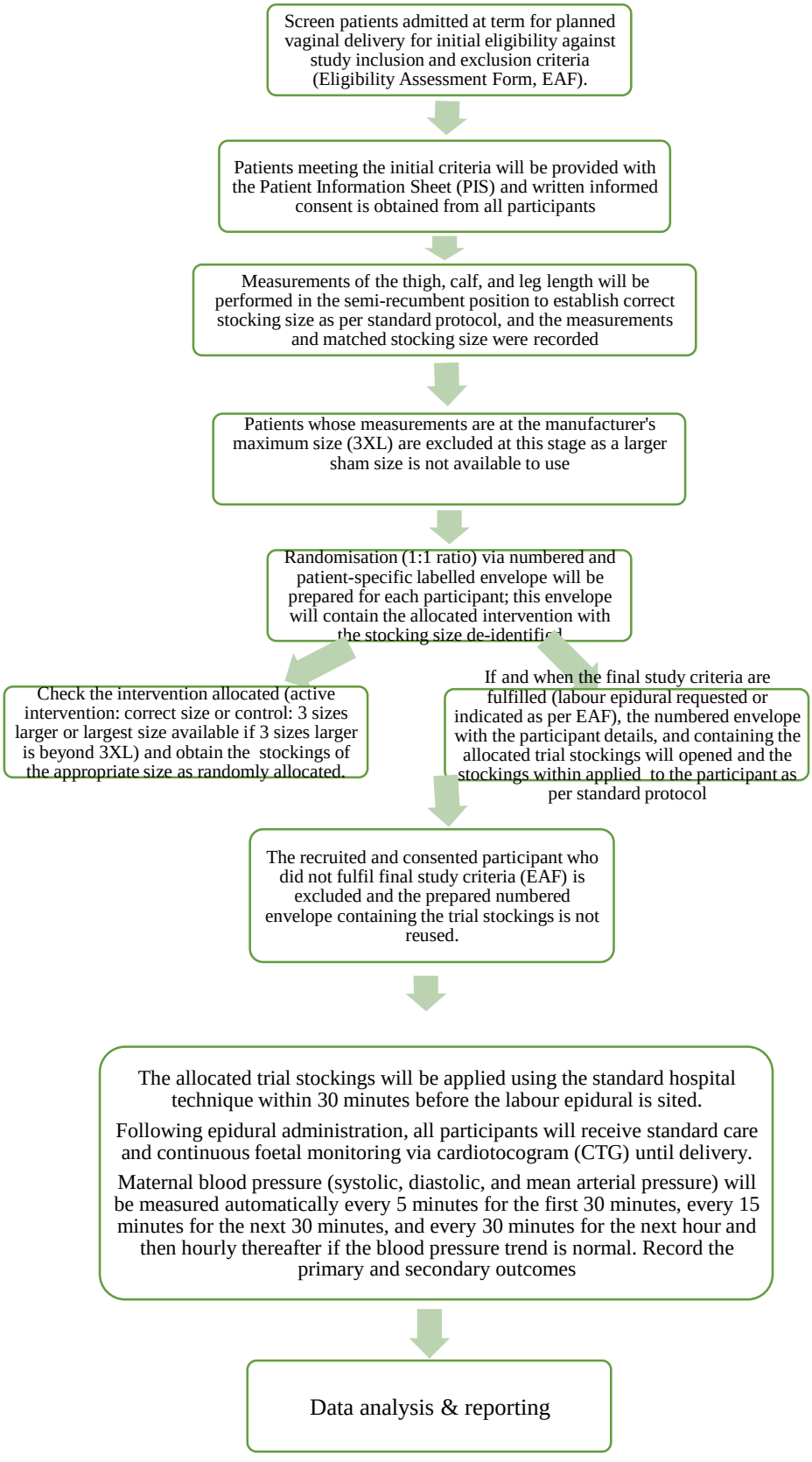
- ✓ Disposable tape measure
- ✓ Antiembolism stocking sizing chart
- ✓ Antiembolism Stockings
- ✓ Mechanical Thromboprophylaxis Care Record Sheet

Action	Rationale
Pre-procedure Perform the stockings **safety checks:** ➢ Is the VTE risk assessment done? ➢ Are the antiembolism stockings prescribed? ➢ Any contraindications noted? ➢ Patient consent for the procedure: explain reasons for wearing antiembolism stockings	All patients admitted to hospital should undergo a risk assessment for venous thrombosis to determine the most appropriate preventive measures, that is thromboprophylaxis[1] The higher the number of risk factors, the greater the risk for VTE[2] To comply with national guidelines and hospital policy/ guidelines. To ensure that antiembolism stockings are used appropriately[3]
Procedure Perform hand hygiene prior to the procedure. **Ideally** take the leg measurements first thing in the morning, with the patient standing up with feet flat on the floor. The tape measure should be snug but not tight, against bare skin. Look at the legs from the back (for length) and from the sides (for girth). Measure both legs separately. The legs should be re-measured: ➢ Post major surgery ➢ Post lower limb surgery ➢ or any other surgery or condition which could cause an increase or reduction in oedema ➢ Maximum after 7 days ➢ On the day of discharge, if prescribed to take home	To prevent cross-infection[4] To obtain the most accurate leg measurements. To ascertain where the widest part of the calves and / or thighs are. To account for differences between right and left leg. To account for changes in leg size during hospital stay.
Measurement For Thigh Length Stockings 1- Measure upper thigh circumference at widest part of thigh 2- Measure calf circumference at greatest dimension. 3- Measure the distance between the gluteal furrow to bottom of the heel 4- Consult the product sizing poster to determine the appropriate size depending on thigh circumference, calf girth and leg length. (a) If right and left legs measure differently, order two different stocking sizes.	To comply with the manufacturer's instructions. Incorrect sizing causes swelling and bruising to ankles and can constrict blood supply, leading to long-term complications. It has also been suggested that 15–20% of patients cannot effectively wear thigh-length antiembolism stockings because of unusual limb size or shape[5] Order 2 pairs to ensure that thromboprophylaxis is

(b) If thigh is greater than that stocked by the manufacturer (91.4cm), knee length stockings may be appropriate. **Measurement For Knee Length Stockings** 1 - Measure calf circumference at greatest dimension 2 - Measure the distance between 1 inch below the knee line to bottom of the heel 3 - Consult the product sizing poster to determine the appropriate size depending on the calf girth and leg length. (a) If right and left legs measure differently, order two different stocking sizes.	uninterrupted during laundering care.  **Thigh Length** **Knee Length**
Applying (a) Insert hand into stocking as far as the heel pocket. (b) Grasp centre of heel pocket and turn stocking inside out to heel area. (c) Position stocking over foot and heel, ensuring patient's heel is centred in heel pocket. (d) Pull a few inches of the stocking up around the ankle and calf. (e) Continue pulling the stocking up the leg as described in manufacturer's instructions. When using thigh length, the top band rests in the gluteal furrow. (f) Smooth out wrinkles. (g) Align inspection window to fall under the toes (toes should not stick out).	To ensure correct size of stocking is fitted correctly. Thigh-length stockings are difficult to put on and can roll down, creating a tourniquet just above the knee which restricts blood supply, so patient monitoring and/or assistance should take place to ensure that stockings are fitted smoothly, are not rolled down or the top band folded down.
Post-procedure Document the **safety checks,** the leg measurements and size of stockings applied in the Mechanical Thromboprophylaxis Care Record Sheet. Provide verbal and written information about the following: (a) how to fit and wear stockings (b) what to report to the nurse, for example any feelings of pain or numbness or skin problems (c) skin care, that is, wash and dry legs daily, applying emollient if clinically indicated (d) reasons for early mobilization and adequate hydration (e) reasons for not crossing legs or ankles – to prevent constriction of blood supply (f) length of time that the stockings should be worn, e.g. stockings should be removed for a maximum of 30 minutes daily and worn until the patient returns to their usual level of mobility.	To ensure that the patient understands how to fit and wear stockings, including self-care measures and what to report to the nurse so as to detect complications early, for example pressure sores, circulation difficulties of wearing antiembolism stockings[6]
Adapted from Dougherty & Lister, 2015 (Royal Marsden Hospital Manual)	

1 - House of Commons Health Committee 2005, C; NICE, 2010a, C; Roderick et al. 2005 , R1a; Scottish Intercollegiate Guidelines Network 2002, C., 2 - NICE 2010, C; Scottish Intercollegiate Guidelines Network 2002, C., 3 - All Wales Tissue Viability Nurse Forum 2009, E; House of Commons Health Committee 2005, C; NICE 2010, C; Rashid et al. 2005, E; Scottish Intercollegiate Guidelines Network 2002, C., 4 - Loveday et al. 2014, C., 5 - Scottish Intercollegiate Guidelines Network 2002, C., 6 - NICE 2010, C; Scottish Intercollegiate Guidelines Network 2002, C.

CHAPTER 4 : PROTOCOL FLOW CHART



CHAPTER 5 : STATISTICAL ANALYSIS

Data will be entered into SPSS statistical software.

CHAPTER 6 : ETHICAL CONSIDERATIONS

This study is submitted to the University of Malaya Medical Centre Medical Research and Ethics committee, the local institutional review board for approval.

KEY MILESTONES OF STUDY ACTIVITY

Data collection	- 6 months
Data analysis	- 3 months
Research presentation	- 2 month
Report submission	- 2 month

GANTT CHART OF STUDY ACTIVITY

Research Activity	**2024**		**2025**		**2026**										
	O	N	N	D	F	M	A	M	J	J	A	S	O	N	D
Literature Review and Proposal Presentation															
Proposal Defence Presentation															
Approval from Ethics Committees															
Data Collection															
Data Analysis/ Interpretation															
Research Presentation															
Report Submission															

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