EFFECT OF SUBCUTANEOUS STERILE WATER INJECTIONS VS NORMAL SALINE INJECTIONS FOR RELIEF OF CONTINUOUS BACK PAIN IN LABOUR AT KENYATTA NATIONAL HOSPITAL. A RANDOMISED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL

Investigator:

Dr.Satbir Singh Karwal
H58/80888/2015
MBChB M. MED Student

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Supervisors:

Dr Alfred Osoti

Consultant Obstetrician and Gynecologist,
Department of Obstetrics and Gynecology,
University of Nairobi

Dr Weston Khisa.

Consultant Obstetrician and Gynecologist,
Department of Obstetrics and Gynecology,
Kenyatta National Hospital

DECLARATION

This study is my original work and has not been presented for a degree in any other University.

Dr. Satbir Singh Karwal

Signed…… Date……

APPROVAL

This proposal has been submitted for examination with the approval of University Supervisors:

Dr Alfred Osoti
Consultant Obstetrician and Gynecologist,
Department of Obstetrics and Gynecology,
University of Nairobi

Signed…… Date……

Dr Weston Khisa.
Consultant Obstetrician and Gynecologist,
Department of Obstetrics and Gynecology,
Kenyatta National Hospital

Signed…… Date……

Prof. Omondi Ogutu
Chairman of Department of Obstetrics and Gynecology,
University of Nairobi.

Signed…… Date……

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I would like to acknowledge the contribution of my family members, staff of the Department of Obstetrics and Gynecology of the University of Nairobi, and my colleagues.

DEDICATION

I dedicate this book to my family for the emotional support accorded during its conception.

LIST OF ABBREVIATIONS

DNIC:	Diffuse Noxious Inhibitory Control system.
DSMC:	Data and safety monitoring committee
CS:	Caesarean Section
IC:	Intracutaneous
INJ:	Injection
KNH:	Kenyatta National Hospital
NSI:	Normal Saline Injections
NRS:	Numerical Rating Scale
PSIS:	Posterior Superior Iliac Spines
RCT:	Randomized Controlled Trial
SQ:	Subcutaneous
SWI:	Sterile Water Injections
TENS:	Transcutaneous Electrical Nerve Stimulation
VAS:	Visual Analogue Scale

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ABSTRACT

Background: Sterile Water Injections (SWI) are ideal for managing continuous labour back pain in the active stage. However, their effectiveness on African parturient and acceptability in African settings is poorly understood. To fill this gap a double blind, placebo controlled, randomised control trial (RCT) was done in an urban hospital setting in Nairobi, Kenya.

Objectives: We evaluated the analgesic effect of SWI on continuous back pain in labour among parturients in the active stage of labour. It also determined the effect of SWI for continuous labor back pains on maternal and neonatal outcomes and its acceptability in the African setting.

Methodology: Parturients confirmed to be admitted in the active stage of labour were recruited and randomly allocated to study groups. A total of 60 parturients (30 in the intervention group and 30 in the control group) were recruited after provision of an informed consent. Parturients in the intervention arm received 0.5ml injections of subcutaneous SWI injections at the four points bordering the Michaelis Rhomboid on the sacral region of the back. The procedure was the same for parturients in the control arm, but using 0.5 ml of 0.9% normal saline solution. Socio-demographic data were recorded. Baseline data on pain perception of parturient was also recorded using a visual analogue scale (VAS) before the administration of injections and 10, 30, 60, 90, and 120 minutes after injections. After delivery, data on adverse maternal and neonatal outcomes were recorded. Mother to baby interaction was evaluated by measuring the time the mother initiated breastfeeding after delivery. The satisfaction of parturients with treatments and whether they might use treatments in future deliveries or recommend them to other parturients was documented. To analyze data, the Statistical Package for Social Scientists (SPSS) software was used. Continuous data were tested for normality using the Shapiro Wilks test and frequency distributions computed. The categorical data were visualized in tables as percentages and mean differences for VAS scores between study groups determined at 10, 30, 60, 90, and 120 minutes using the t test. The t test and Chi-square test were used to compare occurrence of maternal and neonatal outcomes between groups and satisfaction of mothers with SWI or NSI. Statistical significance were interpreted by analysis of P values at the 95% level of confidence ($p<0.05$).

Results: Demographic and reproductive characteristics of parturients were comparable in study groups. At baseline, pain perception, as interpreted by self-reported VAS scores, were similar between the SWI (90 cm) and normal saline (87 cm) groups ($P=0.102$). However, VAS scores at 10 minutes, 30 minutes, 60 minutes, 90 minutes, and 120 minutes were significantly different with women who received SWI for the management of labour back pair reporting significantly less pain perception. SWI did not influence the occurrence of adverse maternal and neonatal outcomes and was viewed as a good mode of pain relief, with 73% more patients in SWI group reporting to be very satisfied with and highly likely to reuse SWI during pregnancies ($P<0.001$)

Conclusion: We have demonstrated the suitability of using SWI for management of continuous labour back pain in African parturient. Administered on the Michaelis Rhomboid on the sacral region of the back, it induces fast and lasting pain relief without adverse pregnancy outcomes.

CHAPTER ONE

1 INTRODUCTION AND LITERATURE REVIEW

1.1 Background

The birth of a child is one of the most significant events in the lives of couples. It brings moments of happiness, joy, excitement and completeness to the family. However, the process also makes mothers anxious, frightened and unwilling to be participative because of the pain associated with labour progression. Many studies rate intensity of labour pain as very severe or unbearable (1,2). Severe labour pain leads to long-term emotional and physical consequences, which often negatively affect the mother's ability to bond with her newborn and her relationship with her partner. It can also cause postpartum depression (3). For women, labour may be their first instance of perceiving severe pain. Relief of pain can improve perception on labour and delivery and influence the process positively.

Around 33% of parturients experience severe continuous back pain in labour (4). This type of pain is distinctive from pain derived from uterine contractions. It is continuous all through labour with no periods of respite. Superimposed with pain of contractions of labour, it intensifies to excruciating levels (5). The fact that severe continuous back pains rarely recede in between contractions, it worsens the experience for women (6).This poses a serious challenge for parturient and their care givers.

1.2 Pathways of Labour Pain

Labour pain are of two broad types - visceral and somatic (7,8). First stage and the second stage of labor constitutes of visceral pain. Uterine contractions cause dilatation of the cervix. As labor progresses, the lower segment of the uterus also distends and activates the excitatory nociceptive afferents in the body (7). These activated afferents innervate both the lower (T10-L1) segments of the uterus and the endocervix. Visceral pain during labor is usually moderate in intensity, dull in character, and is often diffusely located on dermatomes T10-T12 and felt in the sacrum region of the lower back and the abdomen (7,8).

Apart from visceral pain, parturients also experience somatic pain in the late period of first stage of labour and during the second stage of labour. Somatic pain arises as a result of activation of

the afferents that innervate the vagina, perineum, and the walls of the cervix (9). It arises due to distension, ischemia, stretching, and injury to the vagina, perineum, and the pelvic floor. It is also experienced during the descent of the fetus, as the uterine contractions are more pronounced in a rhythmic and regular manner. Unlike visceral pain, which is dull and somewhat moderate, somatic pain is sharp in nature and often localized (8). Pain severity increases with cervical dilatation and is comparable to intensity of uterine contractions

1.3 Transmission of Visceral and Somatic Pain

The unmyelinated 'C' fibers are responsible for visceral pain. In synergy with the sympathetic fibers, they travel through the nerve plexus of the hypogastric, cervix, and uterus and end up in the main sympathetic chain (10). The pain fibers associated with the sympathetic chain enter spinal nerves T10-L1 of the white rami communicants and end up in the posterior nerve roots of the dorsal horn of the spinal cord. Some fibers cross the dorsal horn with extensive caudal and rostral extension, which leads to poorly localized pain. Leukotrienes, bradykinin, lactic acid, serotonin, prostaglandins, and substance P are the chemical mediators of this process (8,11).

Myelinated and fine 'A delta' fibers (rapidly transmitting) transmit somatic pain. Transmission occurs through the perineal branches, pudendal nerves, and the posterior cutaneous nerve of the thigh up to the S2-S4 nerve roots. In cutaneous branches of the genitofemoral and ilioinguinal nerves, somatic fibers carry afferent fibers to L1 & L2 when women are almost delivering (8).

1.4 Methods for Analgesia

Several pharmacological and non-pharmacological methods have been used to relieve labour pain. Some of the most popular pharmacological methods for back labour pain relief include neuroaxial block, parenteral analgesics and inhalational analgesic agents. Neuroaxial labour analgesia is the commonest method used currently. It is the most potent and complete labour analgesia. It includes continuous lumbar epidural technique and combined spinal epidural technique. Continuous lumbar epidural analgesia is the most prevalent pain relieving method in use. It provides very effective labour analgesia. However, studies have shown its link with persistent occiput posterior position, leading to labour dystocia (17, 18, 19). This could be due to alteration of normal mechanism of flexion and rotation of the fatal head, as epidural analgesia

relaxes muscles of the pelvic floor. Epidural analgesia increases risk of instrumental delivery (15,16). Studies have found contradictory link between epidural analgesia and an increase in caesarean section rates (15). Both increase in instrumental deliveries and caesarean section rates are observed more so in nulliparous women. Epidural analgesia is also associated with maternal and fetal fevers (17). During labour, it is difficult to differentiate between infectious and non-infectious fever. Therefore, women who receive epidural analgesia end up more frequently being treated with intrapartum antibiotics. Their infants are also more likely to be evaluated for neonatal sepsis and receive treatment (18). Finally, the risk of intrapartum and postpartum urinary retention increases with epidural use (17,19). This increases the use of urinary catheters, which is a known source of urinary tract infection. Weiniger *et al*. reported an incidence of 30% of urinary tract infections amongst catheterized parturient (19).

Parenteral analgesics are commonly used for labour analgesia in regions where neuroaxial analgesia is not available. They are also used as a combined technique with neuroaxial analgesia. Opiods are the commonest parental labour analgesics used, with pethidine being one of the most administered. Other popular ones fentanyl, tramadol, diamorphine, nalbuphine, remifentanil and butorphanol. The efficacy of opioid analgesia in labour is inferior to neuroaxial analgesia. It is commonly used in women who have contraindications against use of neuroaxial analgesia. Parenteral opioids cross the placenta and cause dose-dependent neonatal, fetal, and or maternal side effects. Sedation, emesis, respiratory depression, and delayed gastric emptying, are common outcomes among mothers, while the commonest side effects on babies include fetal bradycardia, decrease in beat-to-beat variability and neonatal respiratory depression. Results of observational studies have also found effects such as a delayed alertness of babies and inhibited sucking of breasts, which often lead to a delay in effective breastfeeding by babies (22, 23, 24).

Various non-pharmacological methods are available for labour pain analgesia, which include child birth education, emotional and physical therapy support, hypnosis, aroma therapy, hydrotherapy, transcutaneous electric nerve stimulation (TENS), massage, sterile water blocks, and acupuncture. Sterile water injections (SWI), acupuncture and TENS are among the more commonly used techniques, with acupuncture and TENS showing varying degrees of success (24, 25, 26). An RCT by Mårtensson and others compared SWI to acupuncture for labour pain relief, and found that SWI, offers better pain relief during delivery than acupuncture (25).

1.4.1 Sterile Water Injections (SWI)

Systemic reviews, and meta-analysis of randomized control trials (26,27) consistently report a reduction in self-assessed continuous back pain following the use of SWI. These reviews have determined SWI as an effective, simple, cheap and safe method. They have also been used effectively to reduce pain from acute attacks of urolithiasis (28) and neck and shoulder pain (29,30). SWI has not been associated with any side effects. However, previous studies have revealed that it causes a transient intense burning pain during administration that lasts for 20-30 seconds(26). In a study comparing perceived pain during SWI administration via intracutaneous and subcutaneous routes, it was found that subcutaneous SWI injections cause less pain (31).

1.4.2 Mechanisms of Action of SWI

The analgesic mechanism of sterile water injections is not fully known. However, the following theories have been postulated. In Gate Control theory of pain (3), Melzack and Wall, explained how stimuli that activates non-nociceptive nerves can offer pain relief. The theory states that nociceptor (pain fibers) and non-nociceptor (touch, pressure, vibration) fibers synapse in two distinct locations within the dorsal horn of spinal cord. These are cells in the substantia gelatinosa and the 'transmission' cells. According to the theory, the dorsal horn has a gate – the substantia gelatinosa, which controls how sensory information is transferred to the transmission cells in spinal cord from the primary afferent neurons. The activity of the small and large fibers controls the mechanism of this gate. The activity of large fibers closes the gate, while those of small-fiber facilitates the opening of the gate. Small fibers consist of A delta and C fibers while large fibers are the non-nociceptive fibers. Therefore the relative amount of activity in large and small fibers modulates a spinal gating mechanism (3). SWI is salt-free. Therefore, their administration causes osmotic stimulation and distension pain in the cutaneous layer, stimulating skin nociceptors and mechanoreceptors, conveying signals along large fibers and blocking smaller fibers which carry signals from uterine contractions, thus inhibiting pain transmission to dorsal horn (**Figure 1**).

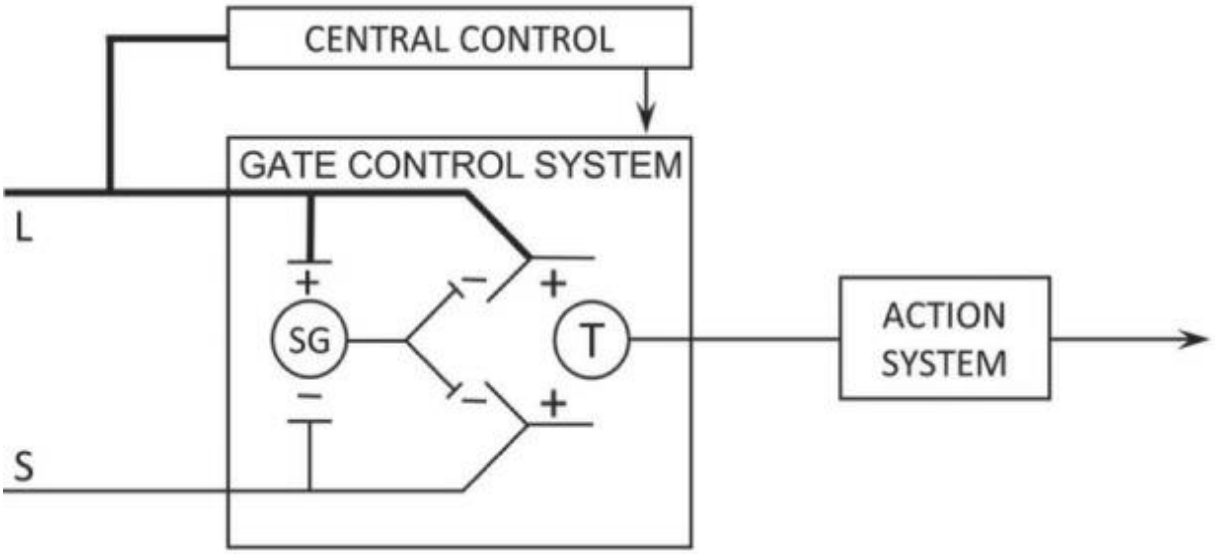


Figure 1: A schematic illustration of the gate control theory of pain proposed by Melzack and Wall (32)

A second theory involves activation of descending pain relief system. Painful stimulus stimulates the production of endogenous opioids by central pain inhibitory systems. Sensory signals generated in painful areas of the body ascend to the brain and stimulate peri-aqueductal grey matter to produce neurotensins and endorphins. These signals also stimulate the nucleus raphe magnus to produce serotonin and noradrenalin. All this substances descend back to the dorsal horn and inhibit nociceptive transmission, at the spinal level, by inhibiting the release of transmitters of primary afferents, inhibiting the projection neurons through a direct post-synaptic action and by exciting inhibitory interneurons and inhibiting excitatory interneurons (26). The third theory postulates that SWI could activate the Diffuse Noxious Inhibitory Control system (DNIC). It is based on the broad concept that spatially distant noxious stimuli can inhibit painful stimulus. Le Bars postulated that physiological activation of brain structures that are responsible for descending inhibition can also activate the DNIC system (26,33,34).

1.4.3 Reviews of Studies on SWI as a Labour Analgesia Method

Table 1: Summary of studies of sterile water injections as relief for labor pain.					
Author /Country	**Objective**	**Inclusion Criteria**	**Design**	**Measuring instrument**	**Results**
Ader *et al*. 1990. Sweden n=45	To investigate the efficacy of sterile water papules for back pain during labor.	-Preg wk> 37, -1st stage of labor, -Back pain, -Require Pain relief, -No prior analgesia in 3hrs.	RCT, double blind, placebo controlled, parallel group. *Study group* n=24, 4x0.1 ml ic SWI *Control group* n=21, 4x0.1 ml sc saline inj	VAS, Pain measured at baseline,10 , 45 and 90 min after inj.	The mean VAS score was significantly lower in the SWI group compared with saline group at 10, 45 and 90 minutes.
Trolle *et al*, 1991. Denmark. n=272	To evaluate the analgesic effect of intradermal SWI for low back pain during labor.	-Active labor, -Severe low back pain.	RCT, double blind, placebo controlled, parallel group. *Study group* n=141 4x0.1 mI Ic SWI. *Control group* n=131 4x0.1 ml ic saline inj.	VAS, Pain measured at baseline,60 , and 120min after inj.	Mean pain score was significantly lower at 60 and 120 min.
Martensson , 1999. Sweden. n=99	To evaluate labor pain relief with sq SWI, and ic SWI vs placebo.	-Preg at 37-42wk , -1st stage of labor, -Severe low back pain, -No prior analgesia in 3hrs	RCT, double blind, placebo controlled, parallel group. *Study group* 1 n= 33 4×0.1 ml ic	VAS, Pain measured at baseline, 10, 45 and 90 min after inj	Median pain scores were significantly lower in the two study groups using SWI compared with placebo. The pain of inj administration

			SWI, Study group 2 n=33 4×0.5ml sq SWI, *Control group* n=33 4×0.1 ml isotonic sq saline inj		was least in Sq SWI group.
Bahasadri, 2006, Iran. n=100	To valuate efficacy of sq SWI in reduction of labor pain compared with placebo.	-Term pregnancy, -1st stage labor, -Low back pain, -No prior analgesia	Randomized, double blind, placebo controlled, parallel group *Study group* n=50 1×0.5ml sq SWI *Control group* n=50 1×0.5ml sq NS inj	Face rating scale, Pain measured at baseline, 10 and 45 min after inj	Median pain score in the SWI group was significantly lower than the placebo group at 10 and 45mins
Wiruchpong-sanon, 2006. Thailand. n=50	To study effectiveness of ic SWI to relieve low back pain during labor.	-Preg at 37-42 wk, -Active phase of 1st stage of labor, -Severe low back pain, -No prior analgesia in 3hrs	RCT, double blind, placebo controlled, parallel group. Study group n=25 4x0.1 ml ic SWI. Control group n=25 4x0.1 ml ic saline inj	VAS, Pain measured at baseline, 30, 60 and 120 min after inj	Mean pain scores were significantly lower in the ic SWI group at 30, 60 and 120 min.
Kushtagi, 2009. India. n=100	To study effectiveness of subcutaneous SWI to lower	-Early active labor, -Low back pain, -No prior	RCT, double blind, placebo controlled,	NRS, Pain measured at baseline,10, and 45	Median pain score was significantly lower in the SWI group.

	back for pain relief in labor.	analgesia	parallel group. Study group n=50 1x0.1 ml sq SWI. Control group n=50 4x0.1 ml sq saline.	min after inj,	
Lee, 2012. Australia. n=266	To evaluate the degree and duration of analgesia provided by a single injection of sterile water, compared to 4 injections.	-Preg at 37-42 -Singleton pregnancy, -Cephalic presentation, -1st stage labor -No prior analgesia, -Back pain by VAS as ≥7,	A randomized, controlled, non-inferiority design. Study group 1 n=133 1x0.1 ml sq SWI.	VAS, Pain measured at baseline, 10,30, 60, 90 and 120 min after inj	Mean pain scores of post-injection were lower than pre-injection in both groups. Mean pain score were lower in the group that received four Inj at one time compared to the group with single inj.
Rai *et al*, 2013. Nepal. n=240	To evaluate effectiveness of subcutaneous SWI versus a placebo in reduction of labor pain.	-Preg at >37 wks, -No prior analgesia, -Low back pain ≥ 7 at enrolment. -No previous uterine scar	RCT, single blind, placebo controlled, parallel group. Study group n=120 4x0.1 ml sq SWI. Control group n=120	VAS, Pain measured at baseline, 10, 45 and 90 min after inj	Mean pain scores were significantly lower in the ic SWI group at 10, 45 and 90 min.
Farag, 2015. Egypt. n=60	To re-evaluate the role of intracutaneous SWI as a method of back pain relief during labor compared to	Age 20 -35 years, Spontaneous vaginal delivery, -Primiparous -Singleton live fetus, -vertex presentation,	RCT, double blind, placebo controlled, parallel group. Study group n=40 4x0.1	VAS, Pain measured at baseline, 10, 45 and 90 min after inj	Mean pain scores were significantly lower in the ic SWI group at 10, 45 and 90 min.

	placebo.	-Preg at 37-40 wks, Spontaneous active labor. -Low back pain ≥ 7 at enrollment.	ml sq SWI. Control group n=20 4x0.1 ml sq saline.		
Tyseer Marzouk, 2015. Egypt. n=63	To evaluate the effect of subcutaneous SWI at the lumbosacral region on labor back pain.	-Age 20 -35 years, Spontaneous vaginal delivery, -Parity of ≤ 3, -Singleton pregnancy-vertex presentation, -Preg at 37-42 -Active 1st stage of labor.	A quasi-experimental (pre-test/ post-test) design. Study group n=63 4x 0.5 ml sq SWI.	-NRS. Pain measured at baseline,10 , 60 , 120 and 180 min after inj, -5 point Likert scale for pain relief satisfaction score	Mean pain score was significantly lower in SWI group. 87.3% of the parturients reported to be strongly satisfied with SWI as method of labor analgesia
Refika Koyucu. 2018. Turkey n=168	To assess the satisfaction level and effectiveness of sterile water injection for back pain among women in labour.	-Aged 18-35 years • 3-42 wks of gestation • vaginal delivery • Cephalic presentation • Single, healthy foetus • Spontaneous onset of labour • Active phase of the 1st stage of labour (3-7 cm cervical dilatation) • Severe low back pain VAS >7cm • Required pain relief	RCT, double blind, placebo controlled, parallel group. Study group n=84 4x0.1 ml sq SWI. Control group n=84 4x0.1 ml sq NSI.	VAS measured at 10,30,60,120, 180 min.	Mean pain score was significantly lower in SWI group.

Many studies have been conducted on the use of SWI for labor pain relief. These include RCT, systemic reviews and meta-analysis. A RCT was conducted by Martensson *et al*. (1999), which compared two different techniques (intradermal vs subcutaneous) of SWI against NSI as control group (31). The study was double blind with a sample of 99 subjects. The VAS was used to assess the levels of pain at baseline, 10 minutes, 45 minutes and 90 minutes. It showed that the median pain scores were significantly lower in the two study groups using SWI compared with placebo.

Two studies done by Ader in Sweden (35) and Trolle in Denmark (36) also had similar findings. These were both double blind, placebo controlled, RCT and also used the VAS to assess the pain scores. They both found mean scores of pain in the SWI compared to the control group to be significantly lower. Two other RCT studies, one done by Bahasadri in Iran (37) and the other by Kushtagi and Bhanu in India (38), used alternative techniques, a single injection, for assessing pain scores. Bahasadri used the Face rating scale, while Kushtagi used the numerical rating scale. Both found median pain scores to be significantly lower in the study groups compared to control groups. An RCT comparing a single injection to the common four injection technique concluded that four injections is a more effective analgesia for a longer duration (39).

Recently in 2013, studies were done in Nepal by Rai (40) and in 2015 in Egypt by Tyseer *et al*. (2015) (41). Rai conducted a single blind, placebo controlled, RCT, which compared 120 participants who were administered SWI against 120 participants who received NSI. The study assessed pain using the VAS and found mean pain scores were significantly lower in the SWI group. Tyseer carried out a quasi-experimental (pre-test/post-test) study. The study was carried out on 63 participants and used the numerical rating scale to assess pain up to 3 hours post injection. Mean pain score were significantly lower in SWI group post injection. The study also evaluated satisfaction rate for labour back pain relief from the subcutaneous injections of sterile water. It found that 87.3% of patients were strongly satisfied with SWI for labour analgesia.

A meta-analysis by Hutton *et al.* (6) on use of SWI for labour pain (6) found that SWI significantly lowered pain scores compared to a placebo, TENS, and acupuncture. Another meta-analysis was carried by Derry *et al*. (8). It analysed seven RCTs. The meta-analysis concluded

that more evidence is required to confirm (or refute) the efficacy of sterile water injections to relieve labour pain. It also recommended methodologically sound RCTs to be done with adequate statistical power to evaluate use of SWI for labour pain relief.

1.5 Conceptual Framework

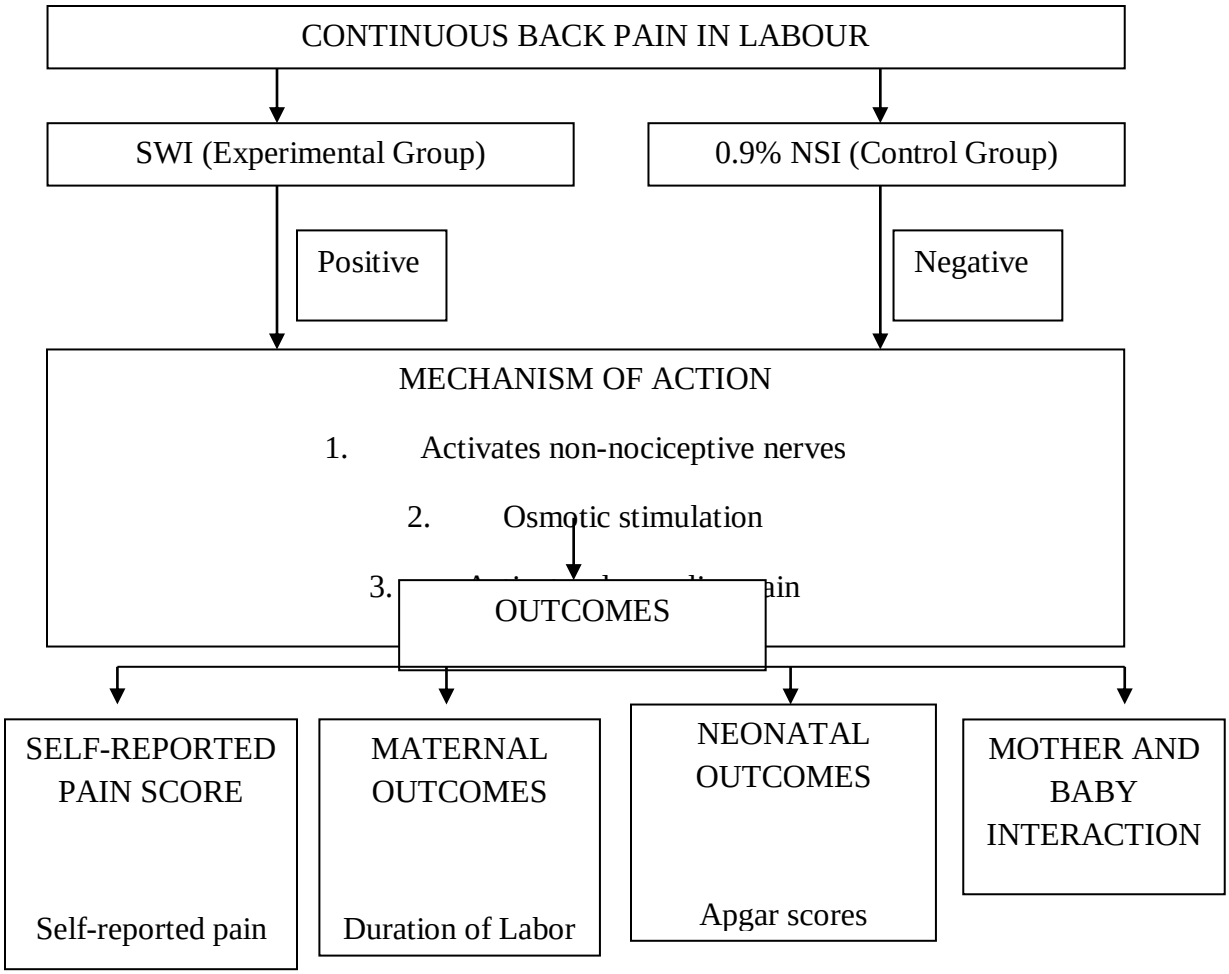


Figure 2: Conceptual framework for proposed RCT

1.5.1 Conceptual Framework Narrative

The management of continuous back pain during labour is a complex process. The type and mode of analgesia that patients receive influences labour progression. To determine the effectiveness and suitability of SWIs for managing continuous back pain in active labour, we tried to minimize biases. We recruited parturients with comparable baseline characteristics (parity, education level, and socio economic status). Allocation of parturients to test and control groups was random. Administration of SWI results in osmotic stimulation and distension pain,

stimulating skin nociceptors and mechanoreceptors, conveying signals along large fibers and blocking the smaller fibers which are carrying signals from uterine contractions, thus inhibiting pain transmission to the dorsal horn. The placebo, 0.9% Normal saline has no such effect. SWIs data was compared with normal saline (0.9%). Data capture tools and procedures used were similar for both groups. The effects of SWI and NSI on relief of self-reported continuous labour back pain was evaluated using VAS scores. Their effects on maternal and neonatal outcome and on maternal-baby interaction were also assessed.

1.6 Study justification

Pharmacological methods have been proven to be potent labour analgesic methods. However, they are associated with several adverse events for parturients and neonates. This has hampered their universal adoption. In most countries, their use is individualized in patients based on benefits against harm. Epidural analgesia is the commonest method used. However, it has been shown to induce numerous untoward effects which include motor blockade, long term backache, hypotension, and decrease in mobility of the laboring parturients. It also increases the risk of labour dystocia, assisted vaginal deliveries, maternal fevers, fetal fevers and urinary incontinence among parturients (15). Systemic pharmacological drugs commonly used are opioids such as pethidine, fentanyl, morphine etc. These are also associated with maternal, fetal and neonatal adverse effects as discussed earlier. Due to fear of these associated side effects, some women do not opt for pharmacological pain relief methods in labour.

Developing countries have limited financial, technical, infrastructural and human resources. Pharmacological pain relief methods are expensive and not readily available, especially in remote areas. Epidural analgesia requires skilled personnel to administer and close monitoring. Therefore, for some women who desire epidural analgesia, this approach may not be available because of the nature of expertise it requires and the cost of equipment, drugs, and human resource requirement. These put pressure on the health sector system. In most developing countries, especially in public health institutions, there are no alternative pharmacological labor analgesia. There is a need to find a safe, affordable, and effective pharmacological analgesia for continuous labour pain, which is also accessible and acceptable in rural and urban settings.

SWI are inexpensive remedies for continuous labour back pain that neither need special equipment nor skills to store and administer. Medical personnel with basic clinical skills can administer SWI effectively with minimal training. Studies have not shown their use to be associated with adverse side effects or interference with labour progression. Furthermore, they do not limit the ability of parturients to move about whilst in labour (6,38,42,43). This makes SWI an optimal pain relief choice for parturients with continuous labour pains.

Data on the use of SWI analgesia in the African population is limited. To our knowledge, no study has been done on the African population. We filled these gaps. We intended to determine the efficacy of SWI on African parturients.

1.7 Research Question

For women experiencing continuous back pain during labour, do subcutaneous injections of sterile water result in a reduction in self-reported pain compared to normal saline?

1.8 Hypotheses

Hypothesis H_0: There is no difference in self-reported pain scores between the intervention and control groups

1.9 Objectives

1.10 Broad objective

To determine the effect of subcutaneous SWI on continuous labour back pain among parturients in the first stage of labour.

1.11 Specific Objectives

1. To determine the effect of subcutaneous SWIs on:
    - Continuous labour back pains in parturients in active stage of labour evaluated using the Visual Analogue Scale.
    - Mode of delivery of pregnancy
    - Maternal outcomes of pregnancy
    - Neonatal outcomes of pregnancy

- Mother to baby interaction

2. To evaluate the satisfaction of Kenyan parturient with subcutaneous SWIs for continuous labour back pains using the five point Likert Scale.

CHAPTER TWO

2 METHODOLOGY

2.1 Study Design

A double blinded, placebo-controlled, parallel group Randomized Control Trial (RCT).

2.2 Study Site and Setting

The study was done at the labour ward, Department of Obstetrics and Gynecology of Kenyatta National Hospital (KNH) in Nairobi, Kenya. This is the largest referral hospital in Kenya, which also has one of the largest and busiest labor wards in the country. Majority of the patients it serves are low to middle income earners from peri-urban areas of Nairobi and its environs. Approximately 500 babies are born at KNH monthly, which accounts for 40% of babies born in Nairobi. No standard care is offered for pain management during labour at KNH.

2.3 Study Population

We targeted all Kenyan women in labour pain who presented themselves at KNH for delivery. Women were admitted at the labour ward at KNH in an active phase of labour and satisfied our criteria for inclusion before recruitment.

2.3.1 Inclusion Criteria

Parturient with a singleton pregnancy and in the active phase of labour qualified for this study. Moreover, all parturient were able to assess their level of labour-induced back pain (continuous) using the Visual Analogue Scale (VAS) (44) and fulfilled the following criteria:

- Were in spontaneous active labour (4-10 cm cervical dilatation)
- Had a gestation between 37 and 42 weeks
- Presented with a fetus in a vertex presentation
- Perceived continuous labour back pain using VAS as being greater than 7

During recruitment, we did not have restrictions on age, parity, and or the weight of parturient.

2.3.2 Exclusion Criteria

Parturient were considered unsuitable for our study if they presented with these attributes:

- Had multiple pregnancies (more than one neonate)
- Received pain management three hours before admission
- Had previous pelvic surgeries (myomectomy and caesarean section (CS))
- Had contraindications for vaginal delivery (assisted or normal)
- Had fetal mal-presentations (breech, transverse, shoulder)
- Had infections at the lumbo-sacral region of the lower back
- Has obstetric complications such as abruption placenta, placenta previa, and cephalopelvic disproportion
- Had associated debilitating diseases such as cardiac disease and kidney disease
- Had a non-reassuring Fetal status (NRFS)

2.4 Sample Size Calculation

We adopted a statistics formula reviewed by Zhong(45) (**Figure 1**) to determine sample size.

$$N = 2 \times \left(\frac{z_{1-\frac{\alpha}{2}} + Z_{1-\beta}}{\delta} \right)^2 \times s^2$$

Figure 3: Formula for determining sample size for statistical significance (N) in RCT studies

Where:

$Z_{1-\alpha/2}$ = the standard normal deviate for α (1.96)

$Z_{1-\beta}$ = the standard normal deviate for β (0.84)

S= polled standard deviation of both comparison groups (2.2)

δ = real difference between the effect of two treatments (2)

Farage *et al*. (5) reported a mean difference (δ) of two points in VAS after 45 minutes in parturient receiving sterile water blocks and a placebo. Farage *et al.* (43) also reported a standard deviation of 2.2 in a RCT on the same. We used these data for sample size (N) calculation. To

demonstrate 20% mean difference between pre and 30 minutes after injection VAS scores with 80% power and a significance level of 0.05, we required 21 participants in each study group. The sample size calculator for continuous measurement of two samples (http://www.sample-size.net/sample-size-means) were used for calculations. Yu *et al*., (2010) recommended a sample size adjustment of 20%-30% to cater for unexpected events. We used 20% to account for attrition or early births. Thus, 52 parturient (26 in each group) were needed. To achieve a normal distribution, we targeted 30 subjects per group as was recommended (47).

2.5 Sampling Procedure

A modified protocol by Lee *et al.* (12) was used to recruit participants. Ampoules of sterile water injections (n=30) and 0.9% normal saline (n=30) were obtained. Ampoules were blinded by first removing their labels. Numbers (1-60) were uploaded into the QuickCalcs number generator (GraphPad Software at https://www.graphpad.com/quickcalcs) and its system used to generate two groups (A and B) of 30 unique numbers. To minimize bias, this process was carried out by an independent statistician, who was not to be involved in the recruitment, administration of injections, and in data analysis. The first group of random numbers were coded for the experimental group in a password protected database and used to label ampoules of sterile water injections (SWI). The numbers in the second group were coded for the control group in a password protected databases and used to label ampoules of 0.9% normal saline. Either of the two groups were labeled and presented as A or B to blind our data analysis team and other research members. They were not be aware of the corresponding study group for data assigned to group A and group B and therefore analyze data unaware of what group A and B represents. Only the independent statistician was aware of this data and disclosed it only for reporting purposes after data analysis. All ampoules were packaged in single study packs (including a questionnaire, test or control vial, and a 2ml syringe with 23-gauge needle). Both the questionnaires and the packs were pre-labelled with the number of the ampoule, which were also used as the study number of participants. Randomization of parturient into study arms was done using study packs. These were arranged in a chronological order (1-60) and issued to patients who consented for inclusion in the study as they were received at the KNH labor ward.

Normal saline injections (NSI) were included as the placebo arm in this study to ensure that the results reflect the real effects of the intervention (i.e. SWI) that we administered. Patients often have good expectations whenever they receive interventions for pain relief. It was therefore necessary to ascertain that the intervention, SWI in our case, had a real and not a 'placebo effect'. A placebo effect occurs when an inactive intervention gives positive results based on a person's perception of the treatment. Thus, in this study, it is necessary that participants in both arms are injected to eliminate the possibility of SWI injections having a placebo effect.

Having NSI as the placebo arm also assures that patients and research investigators are blinded on treatment assignment to lower bias. All prior RCT have used Normal saline injections as placebo (9, 10, 16, 29, 37), and none has reported severe adverse effects. No prior studies have shown NSI, when used as placebo, to worsen maternal and neonatal outcomes (9, 10, 16, 29, 37). Patients in placebo arm were recruited randomly and no double standard was applied.

2.6 Data Management

2.6.1 Data Variables

The pain levels of parturient, measured by VAS for SWI or NSI (0.9%) were our main outcome variables. These were recorded at different intervals (before injection and 10, 30, 60, 90, and 120 minutes after injection) to track the progress of labour pain. Secondary outcomes were the adverse maternal and adverse neonatal outcomes of labour. These included complications such as a retained placenta or hemorrhage and low APGAR scores of neonates. We tested the satisfaction of parturient with the analgesic effect of sterile water blocks or the placebo (normal saline). We also assessed mother to baby interaction by measuring the time before a mother initiates breastfeeding after delivery. Our main independent variable was the intervention that parturients received. Baseline data such as the gestation of parturient, BMI, and gravidity of parturient were our other independent variables. These are highlighted in detail in **Table 2**.

Table 2: Outcome and independent variables of our study and their characteristics

OUTCOME VARIABLES		**DATA TYPE**
PRIMARY OUTCOME		
(1) Pain Perception/Level (VAS)	▪ Pain before injections	Continuous
	▪ Pain at 10min after injection	
	▪ Pain at 30min after injection	
	▪ Pain at 60min after injection	
	▪ Pain at 90min after injection	
	▪ Pain at 120min after injection	
SECONDARY OUTCOMES		
(2) Mode of Delivery	▪ SVD ▪ Vacuum ▪ Caesarean Section	Dichotomous
(3) Duration of Labor (minutes)	▪ Active first stage ▪ Second stage	Continuous
(4) Adverse Maternal Outcomes	▪ Post-partum hemorrhage	Dichotomous
	▪ Retained Placenta	Dichotomous
	▪ HDU/ICU referral	Dichotomous
	▪ Mortality	Dichotomous
(5) Adverse neonatal outcomes	▪ Apgar score at 1 minute	Continuous
	▪ Apgar score at 5 minutes	
	▪ Apgar score at 10 minutes	
	▪ Admission to NCIU	Dichotomous
(6) Mother to child interaction	▪ Time from delivery to initiation of breast feeding	Continuous
(7) Satisfaction Assessment	▪ Satisfaction with interventions	Dichotomous
	▪ Re-use of interventions	
	▪ Recommendation of injections	
INDEPENDENT VARIABLES		**DATA TYPE**
(1) Pain Intervention	▪ SW1	Dichotomous
	▪ NSI	
(2) Age	▪ Age in years	Continuous
(3) Education Status	▪ Illiterate	Dichotomous
	▪ Primary	
	▪ Secondary	
	▪ Tertiary	
(4)Marital Status	▪ Married	Dichotomous
	▪ Single	
	▪ Divorced	
	▪ Widowed	
(5) Body Mass Index	▪ BMI	Continuous
(6) Gravida	▪ Gravida	Continuous
(7) Gestation	▪ Gestation in weeks	Continuous

2.7 Data Collection Procedures

2.7.1 Recruitment of Parturient

Informed consent was sought from parturients admitted in KNH labour ward by a trained midwife. Printed study participation and consent forms were issued to potential participants in the active phase of labour (cervical dilation of greater than 4 cm) and the parturients given time to review the document. The consent form captured our objectives. The potential risks and benefits of this study were also highlighted. Parturient who could not read were assisted by a relative or an accompanying helper of her choice. A question and answer session was held and questions or concerns of parturient were addressed before signing the consent form. During this stage, we stressed the concept of autonomy of parturient. We also stressed the concept of voluntarily participation and that the participants were eligible to drop out of study at any given time and would continue to receive standard care of labour. Participants were informed that they could request other options of routine pain relieving methods available at the hospital. After informed consent, parturient were allotted to either study or control arm using study packs.

Women in Labour, like the normal population, have the capacity to provide informed consent. There are concerns that women in labour may be vulnerable (48). However, evidence from several studies shows that parturients are capable of giving informed consent and that labour pain, anxiety, and duration of pain do not influence a women's ability to understand the risks of study involvement. Other studies have shown that the recall of risks of study interventions is similar to that of other patient groups (49). A study by Dorantes evaluated if the environment during the labour process is coercive for giving informed consent. It concluded that the most vital factors that can influence a patient's decision to consent were related to their understanding and alleged importance of studies and benefits to other women and not pressure to consent (50).

2.7.2 Blinding

Blinding was at two levels. Parturient did not know the study arm they were allotted nor the type of intervention they received for labour pains. The midwife administering interventions and personnel involved in data collection, entry and analysis were not aware of allotted groups.

2.7.3 Data Collection

Three tools were used to collect data. First, after the recruitment of parturient and allocation into study arms, a pretested questionnaire was used to capture demographic data of parturient. These included marital status, age, height, weight and occupation. Obstetric information of parturient such as gestation by date, parity, and gravidity were also captured on this tool (**Appendix 1**). Second, the Visual Analogue Scale (VAS) (**Appendix 2**) was used to assess level of continuous labour back pain of parturient. VAS is a sensitive tool for assessing labour pain. Its psychometric response scale is easy to administer and score. Even in labour, most parturient can complete it in less than one minute with little training (43). The VAS tool was administered five times over the duration of our experiments (before injection with the intervention or placebo (at baseline) and 10, 30, 60, 90, and 120 minutes) to track progression of labour pain. Following a procedure by Lee *et al*. (12), injections were administered to parturient using standard protocol.

Briefly, parturient were placed in a sitting position. Four (4) subcutaneous injections were administered at the Michaelis Rhomboid on the sacral region using a 2ml syringe with a 23-gauge needle (**Figure 2**). Parturient in intervention group received 0.5 ml injections of sterile water blocks. The first two injections were in the Posterior Superior Iliac Spines (PSIS) of sacral areas of the lower back. The third and fourth injections were three centimeters below and 1 centimeter medial of the PSIS. The protocol was the same for the control group using 0.5ml of a 0.9% normal saline solution instead. Standard labour and delivery management guidelines and protocols were followed in care of the participants throughout the study and repeat injections offered on request.

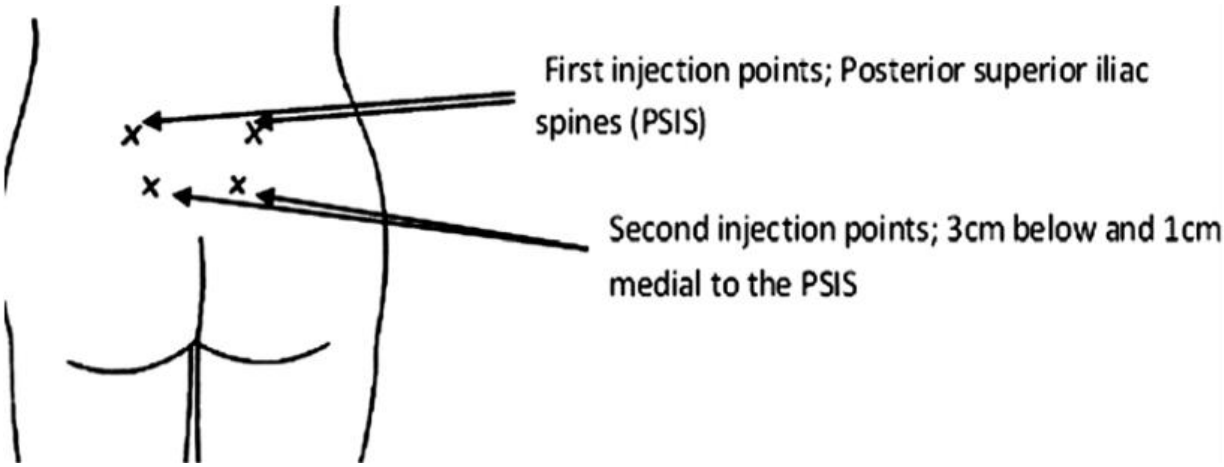


Figure 4: Sites for injection of SWI and NSI on parturient(12)

During labour progression, the adverse maternal and or neonatal outcomes on parturient were recorded on questionnaires by the primary mid wife. Requests for additional pain management injections were recorded. The mid wife also recorded the mode of delivery of parturient and need for interventions such as oxytocin augmentation or of other pain control methods during labour. Adverse neonatal outcomes entailed NBU admissions and Apgar scores at one minute, five minutes, and 10 minutes. To determine the level of satisfaction of parturient with our interventions, a Participant Satisfaction tool (**Appendix 3**) was used to capture data. Satisfaction of continuous back pain relief during labour using SWI and NSI injections were determined using a Likert scale. The scale was from 1-5, with 1 signifying very unsatisfied and 5 very satisfied. The likelihood of parturient using SWI or NSI for labour pain relief in future pregnancies or recommending them to other women were also tested. All revised tools after pretesting, were submitted to the KNH-UON ERC for final vetting and approval before use

2.7.4 Validity of Data Collection Tools

The VAS was our preferred tool for assessing the severity of labour pain during our study. Many studies have demonstrated, to a high degree, that it is a valid and reliable tool for quantifying labour pain (51,52). It is also simple, accurate, and does not require specialized training for interpreting of score. One study (53) found that a score between three and six (30-60mm) reflects moderate pain, while a VAS score of seven (70mm) or more would indicate severe pain. This is consistent with the observations of Peart (54) with regards to parturients in labour who have severe back pain. Overall, linear pain rating scales provide consistent ordinal data with increasing and decreasing levels of pain (53). The validity of questionnaires was determined using the face validity technique (55). The questionnaire and participant satisfaction sheet was shared with senior midwives in KNH labour ward and lecturers at the department of Obstetrics and Gynecology, UoN, for their input. Their comments for improvement were factored into data collection tools before data collection. To ascertain the reliability of research instruments, the test-retest technique was used. Twelve women were recruited from the antenatal clinic at KNH and the questionnaire administered and data extracted and inputted into an SPSS database. All 12 women recruited at baseline were followed up during their next antenatal clinic, the same questionnaire administered, and data entered in an SPSS database. To determine the similarity of responses between the two sampling durations, descriptive statistics were explored and intra-

class correlation coefficients (ICCs) for continuous variables and the Kappa (K) statistic for categorical variables computed. ICCs of continuous variables were interpreted as poor (0.3-0.49), moderate (0.5-0.69) and high (0.7-1.0). The K static was interpreted as being poor (0-0.4), moderate (0.41-0.6), substantial (0.6-0.8) and high (0.81-1.0). Variable with poor scores vetted, redesigned, and retested before data collection.

2.7.5 Data Entry and Storage

Filled data capture tools were filed and locked in a cupboard. A password protected database using Microsoft Access software was generated as backup for data of our study.

2.7.6 Data Analysis Procedure

The normality of continuous data was tested using Shapiro-Wilk test and judged visually using histograms. The t-test was used for normally parametric data and the Man Whitney U test for non-parametric data. Data for categorical outcomes were analysed using chi square test. Baseline data of parturient were computed and assessed to determine comparability between study groups. However formal statistical testing were not done to assess differences. Mean differences and standard deviations (SD) were computed for VAS at baseline, 10, 30, 90, and 120 minutes. The occurrence of adverse maternal and neonatal events between the intervention and the non-intervention groups and satisfaction of parturients with interventions were done and t static for continuous data and Odds Ratios (OR) for categorical variables used to determine statistical significance. This was set at $p<0.05$ for 95% confidence interval (CI) for outcomes.

2.8 Ethical Considerations

2.8.1 Ethical Review

Approval to conduct this study was granted by the Ethics Review board of the University of Nairobi / Kenyatta National Hospital. Permission to carry out this study was also obtained from Department of Reproductive health, KNH and Department of Obstetrics and Gynecology, UON.

2.8.2 Informed Consent

Informed consent was sought from parturient before inclusion in the study or collection of data. Printed consent forms were given to all parturient for review. Consent forms were available in

both English and Kiswahili. If a parturient could not read/write, the consent form was read to her by a relative or a helper of her choice. The consent form covered the objectives, anticipated risks, and benefits of the study, and stressed the concept of voluntary participation. Before recruitment into the study, parturient were allowed to ask questions or seek clarification. A trained midwife answered questions satisfactorily before assigning parturient to study arms.

2.8.3 Staff Training

Special training sessions were held at the Labour ward of KNH before commencement of this study. Midwives and clinical practitioners were educated on study objectives. Demonstrations on how to interpret VAS, select injection site, and administer injections correctly were also done. At KNH, midwives and clinical practitioners are proficient in administering subcutaneous skin injections. However, our trainings minimized bias and enhanced the safety of parturient.

2.8.4 Data Safety and Monitoring

We strived to ensure the confidentiality of parturient. Identifying information such as names and identification details were not be recorded on data collection tools. Random study numbers were used to identify participants. Files were locked in storage and databases password protected. Finally, to ensure data safety and the confidentiality of patients, a Data Safety and Monitoring Committee (DSMC) was formed. This multi-disciplinary board was responsible to review all adverse events associated with the study. The DSMC committee comprised a consultant obstetrician/ gynecologist, a consultant anesthesiologist, a statistician, a senior mid-wife, and research expert. In the case of any complications, participants received appropriate care and had full access to the research team and the committee. The members of the DSMC committee were blinded to treatment allocation. However, they were granted access data whenever a need arose.

2.8.5 Interruption of the Study

To the best of our knowledge, no significant adverse effects nor allergic or systemic reactions have been reported in studies on SWI(42). Moderate transient discomfort for 20-30 seconds after injection is the only untoward effect known. To counteract this, we administered the injections at the peak of uterine contractions. In the case of severe adverse effects, experiments were to be terminated and the principle investigator and safety committee notified following the directions

of the WHO. Briefly, reporting officers were to deliver written adverse event reports to a central address of the safety committee by hand or through web-based protocols such as emails and fax. Since these modes of reporting are widely available in Kenya, we expected the reporting process for patients' adverse events to be seamless. Narrative text in form of comments and a structured form (Appendix 9) was used for adverse event reporting by all reporting officers. The form covered all elements required by the MoH for reporting adverse events such as the diagnosis of patients, dosage, severity of reactions, and the actions taken to prevent permanent injury or to arrest the events. Most of these elements had fields with a cascade of options that reporters checked. These shortened reporting time and improved accuracy. Narrative sections of forms granted reporters the opportunity to offer meaningful insights into the nature of the adverse events and series of study procedures that might have contributed to their development.

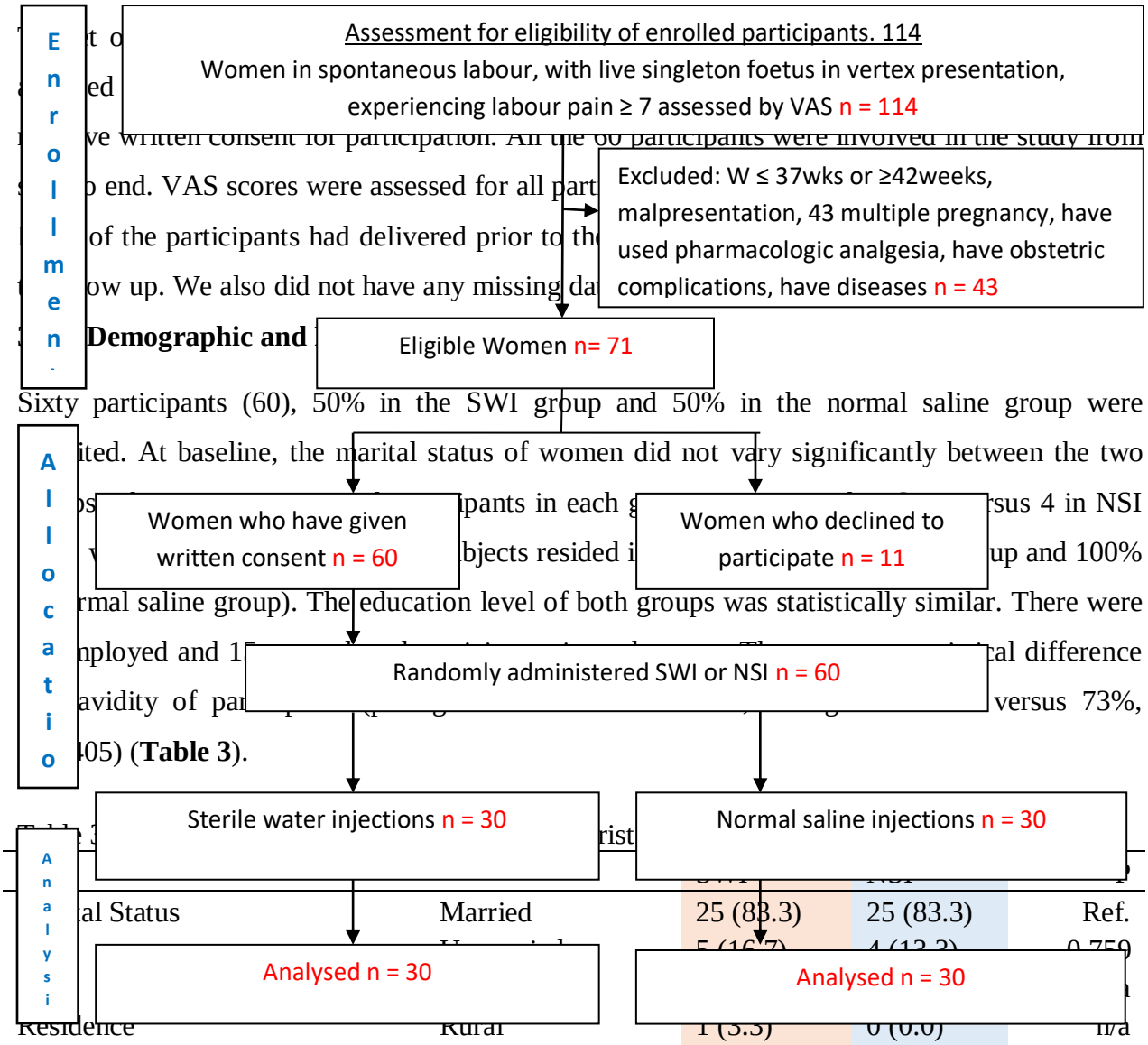
2.9 Study Limitations

This study evaluated pain relief of continuous back pain in labour at intervals of 30 minutes for a total duration of 2 hours from time of injection administration. Therefore it was not be able to test the maximum duration of pain relief the injections could offer. The study did not evaluate the effect of SWI on continuous back labour pain in the latent stage and second stage of labour. More studies could be developed to test if they have any benefits for these phases of labour, as the existing data is limited.

CHAPTER THREE

3 RESULTS

3.1 Consort Flow Diagram



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ve written consent for participation. All the 60 participants were involved in the study from
o end. VAS scores were assessed for all part
of the participants had delivered prior to th
ow up. We also did not have any missing da

Demographic and

Sixty participants (60), 50% in the SWI group and 50% in the normal saline group were
ited. At baseline, the marital status of women did not vary significantly between the two
pants in each g
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rmal saline group). The education level of both groups was statistically similar. There were
nployed and 1
al difference
avidity of par
versus 73%,
405) (**Table 3**).

rist

al Status	Married	25 (83.3)	25 (83.3)	Ref.
Residence	Rural	1 (3.3)	0 (0.0)	n/a
	Urban	29 (96.7)	30 (100.0)	n/a
Education Level	Primary	5 (16.7)	4 (13.3)	0.724
	Secondary	15(50.0)	13 (43.3)	0.724
	Tertiary	10 (33.3)	13 (43.3)	0.724
Occupation	Employed	15 (50.0)	15 (50.0)	1.000
	Unemployed	15(50.0)	15 (50.0)	1.000
Gravidity	Primigravida	11 (36.7)	8(26.7)	0.405
	Multigravida	19 (63.3)	22 (73.3)	0.405

The age of participants (p=0.800), height (p=0.344) and weight (p=0.344) were comparable between the two study groups (Table 4). The gestation of age in weeks (p=0.200) and parity (p=0.499) were also comparable .The cervical dilation of patients at the time of first injection was 6cm in the SWI versus 5 cm in the NSI group, having no statistical difference (**Table 4**).

Table 4: Demographic and Reproductive Characteristics of Participants: N=60

	SWI		NSI		
	M	SD	M	SD	P
Age in Years	25	6	26	5	0.800
Height in CM	157	9	160	6	0.210
Weight in Kgs	77	21	71	10	0.163
Parity	1	1	1	1	0.499
Gestation in weeks	39	2	39	1	0.200
Cervical dilation at first injection (cm)	6	1	5	1	0.541

3.3 Self –Reported Pain Scores

The self-reported pain scores for patients in the SWI group (90) and normal saline group (87) were similar at baseline (p=0.102). However, after 10 minutes, a significant reduction in pain perception was reported in SWI group (52) than normal saline group (78), with the difference being statistically significant (p<0.001). A similar trend was reported at 30 minutes (p<0.001), 60 minutes (p<0.001), 90 minutes (p<0.001), and 120 minutes (p<0.001), with significantly more participants recruited in the SWI group experiencing less pain (**Table 5**).

Table 5: Self-Reported VAS Scores at Baseline and 10/30/60/90/120 Minutes: N=60

	SWI		NSI		
	M	SD	M	SD	P
VAS score at baseline	90	6	87	6	0.101
VAS score at 10 minutes	52	19	77	14	**<0.001**
VAS score at 30 minutes	45	22	80	19	**<0.001**
VAS score at 60 minutes	41	24	80	19	**<0.001**
VAS score at 90 minutes	38	26	82	19	**<0.001**
VAS score at 120 minutes	35	29	84	19	**<0.001**

The VAS scores of participants in the SWI group reduced progressively from baseline, at 10, 30, 60, 90 and 120 minutes. The lowest mean VAS scores of 35 was obtained at 120 min. No such pattern was obtained for the NSI group (**Figure 5**).

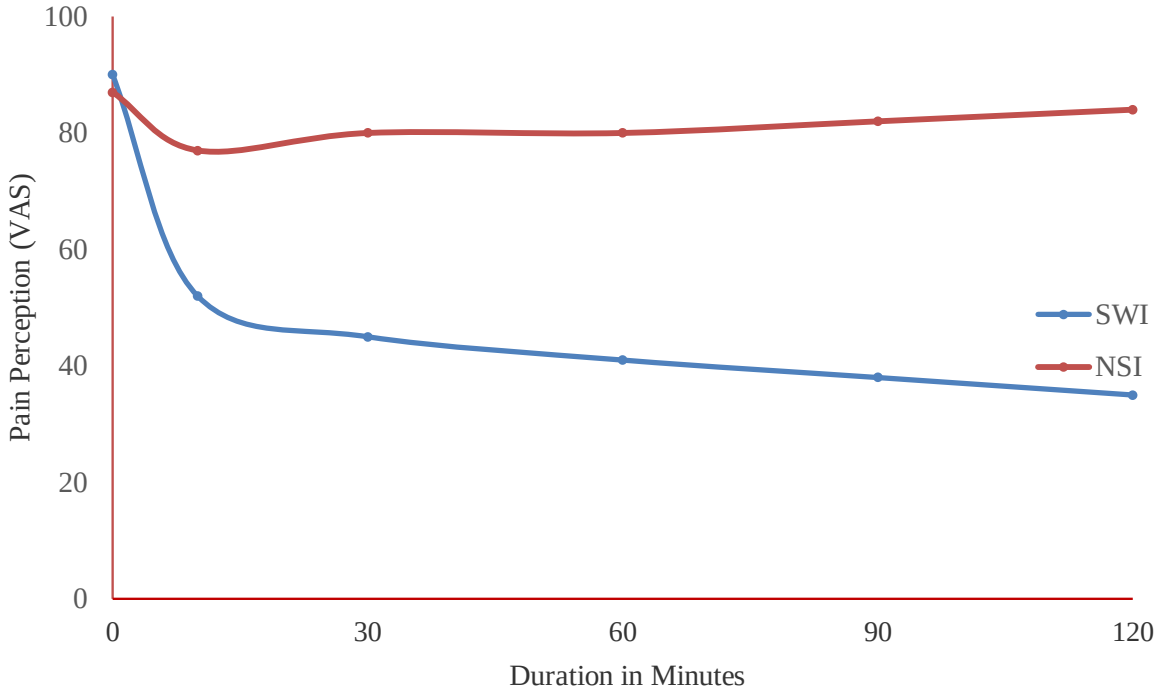

Figure 5: Pain Perception at Baseline, 10, 30, 60, 90, & 120 Minutes

3.4 Pain Reduction of ≥30% and 50%

Twenty three (23) participants in the SWI group had a pain reduction of ≥30% at the 10 min duration, compared to 3 (10.0%) in the NSI group. At the 30, 60, 90 and 120 minute duration the SWI group had 25 participants at each interval, while NSI group had 3 participants at, 90 and 120min duration and 4 participants at the 60 min duration (**Table 5**).

Table 6: Pain relief of ≥30% between intervention and control groups

	≥30% Pain Reduction		
Min	SWI	NSI	P
10	23 (76.7)	3 (10.0)	**<0.001**
30	25 (83.3)	3 (10.0)	**<0.001**
60	25 (83.3)	4 (13.3)	**<0.001**
90	25 (83.3)	3 (10.0)	**<0.001**
120	25 (83.3)	3 (10.0)	**<0.001**

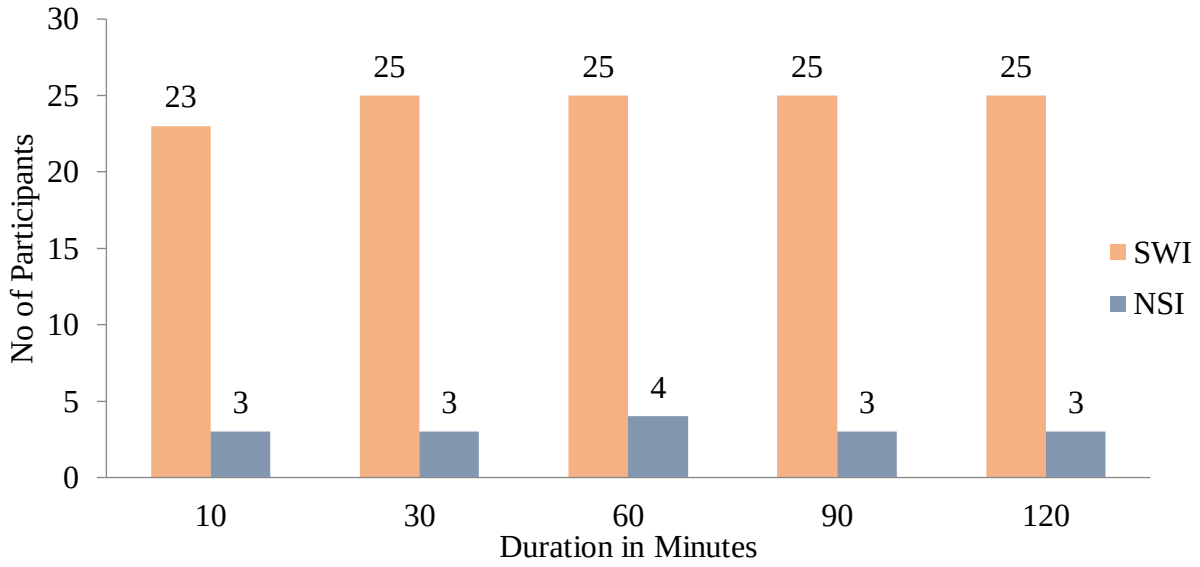

Figure 6: Pain relief of ≥30% between intervention and control groups

Pain reduction of ≥ 50% was also evaluated for both groups. The SWI groups had 16 and 22 participants at 10 minute and 30 minute interval respectively, and 24 participants each at 60, 90 and 120-minute interval. The NSI group had fewer participants with a pain reduction ≥ 50%. SWI group had more participants who experienced ≥ 50% and ≥ 30% pain reduction, with the reported differences being statistically significant at all intervals (p= <0.001) (**Table 6**).

Table 7: Pain relief ≥50% between intervention and control

	≥50% Pain Reduction		
Min	SWI	NSI	P
10	16 (53.3)	1 (3.3)	**<0.001**
30	22 (73.3)	2 (6.7)	**<0.001**
60	24 (80.0)	2 (6.7)	**<0.001**
90	24 (80.0)	1 (3.3)	**<0.001**
120	24 (80.00	1 (3.3)	**<0.001**

3.5 Need for Intra-partum Intervention

The methods of analgesia administered to patients did not influence maternal outcomes. Even though more patients were administered oxytocin in the normal saline group (76.7%) than the SWI group (56.7%), the 20% difference observed was not statistically significant (p=0.100). None of the participants in the SWI and NSI group requested for administration of additional injections. An alternative mode of analgesia was not requested in both study groups (**Table 8**).

Table 8: Need for Intrapartum Interventions

	SWI	NSI	P
Need for augmentation with Oxytocin	17 (56.7)	23 (76.7)	0.100
Request for alternative analgesia	0 (0.0)	0 (0.0)	n/a
Request for additional injections	0 (0.0)	0 (0.0)	n/a

3.6 Maternal Outcomes

The incidence of caesarian deliveries was higher in the normal saline group n=4 (13.3%) than in SWI group n=1 (3.3%), however it was not statistically significant (p=0.161). There were 2 occurrences of PPH in the SWI group and 1 in the NSI group. This was not statistically different (p=0.554). In both groups none of the participants had vacuum assisted delivery. There were also no HDU/ICU admissions and maternal mortalities in both groups (**Table 9**).

Table 9: Maternal Outcomes: N=60

	SWI	NSI	P
Vaginal Deliveries	29 (96.7)	26 (86.7)	
Caesarean delivery	1 (3.3)	4 (13.3)	0.161
Vacuum delivery	0 (0.0)	0 (0.0)	n/a
Post-Partum Hemorrhage (PPH)	2 (6.7)	1 (3.3)	0.554
HDU/ ICU admissions	0 (0.0)	0 (0.0)	n/a
Mortality	0 (0.0)	0 (0.0)	n/a

Mean duration of second stage of labour was 58 minutes in SWI group and 56 minutes in NSI group, which was statistically not different (p=0.784) (**Table 10**).

Table 10: Mean Duration of Second Stage

	SWI		NSI		
	M	SD	M	SD	P
Duration of second stage (minutes)	58	24	56	28	0.784

3.7 Neonatal Outcomes

The methods of analgesia administered to patients did not influence the occurrence of adverse neonatal outcomes. At 1 (p=0.070), 5 (p=0.324), and 10 minutes (p= 0.274), the Apgar scores of babies were comparable between the treatment and control groups. The birth weight of babies

between study groups was also comparable. No peri-natal mortalities were observed in the 24 hour follow-up of neonates in the study (**Table 11**).

Table 11: Neonatal Outcomes: N=60

	SWI		NSI		
	M	SD	M	SD	P
Apgar score at 1 minute	9	1	9	1	0.070
Apgar score at 5 minutes	9	1	9	1	0.324
Apgar score at 10 minutes	10	1	10	0	0.274
Birth weight in grams	3246	500	3261	523	0.908

3.8 Satisfaction with Treatment

The satisfaction of patients was evaluated using a five point Likert scale. With patients who were very unsatisfied with their method of analgesia as a reference, more participants who received SWI injections (66.7%) than those who received normal saline injections (6.7%) were very satisfied with the mode of analgesia. The 60.0% difference reported was statistically significant ($p<0.001$). Among those who were very unsatisfied or unsatisfied, 21 participants were in the NSI group while only 3 were in the SWI group (**Table 12**).

Table 12: Satisfaction with Treatment: N=60

		SWI	NSI	P
Are you satisfied with the method for pain relief?	Very unsatisfied	1 (3.3)	13 (43.3)	Ref.
	Unsatisfied	2 (6.7)	9 (30.0)	0.399
	Neither satisfied nor unsatisfied	4 (13.3)	3 (10.0)	**0.011**
	Satisfied	3 (10.0)	3 (10.0)	**0.028**
	Very satisfied	20 (66.7)	2 (6.7)	**<0.001**

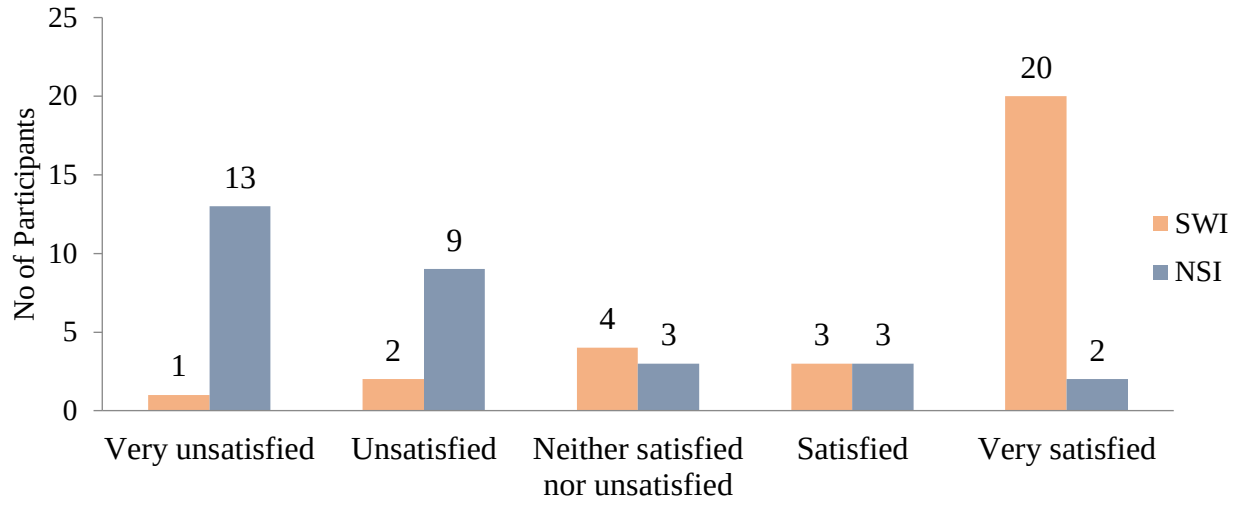

Figure 7¨ Satisfaction with Treatment among Patients in SWI and NSI Group

More patients in the SWI group (66.7%) than in normal saline group (6.7%) were highly likely to reuse the method of analgesia, with the 60.0% difference being significant (p<0.001).

Table 13: Likelihood of Reusing Method of Analgesia: N=60

		SWI	NSI	P
Likely are you to use the same method of Labour pain?	Highly unlikely	1 (3.3)	13 (43.3)	Ref.
	Unlikely	3 (10.00	10 (33.3)	0.244
	Neither likely nor unlikely	2 (6.7)	1 (3.3)	**0.014**
	Likely	4 (12.3)	4 (13.3)	**0.021**
	Highly likely	20 (66.7)	2 (6.7)	**<0.001**

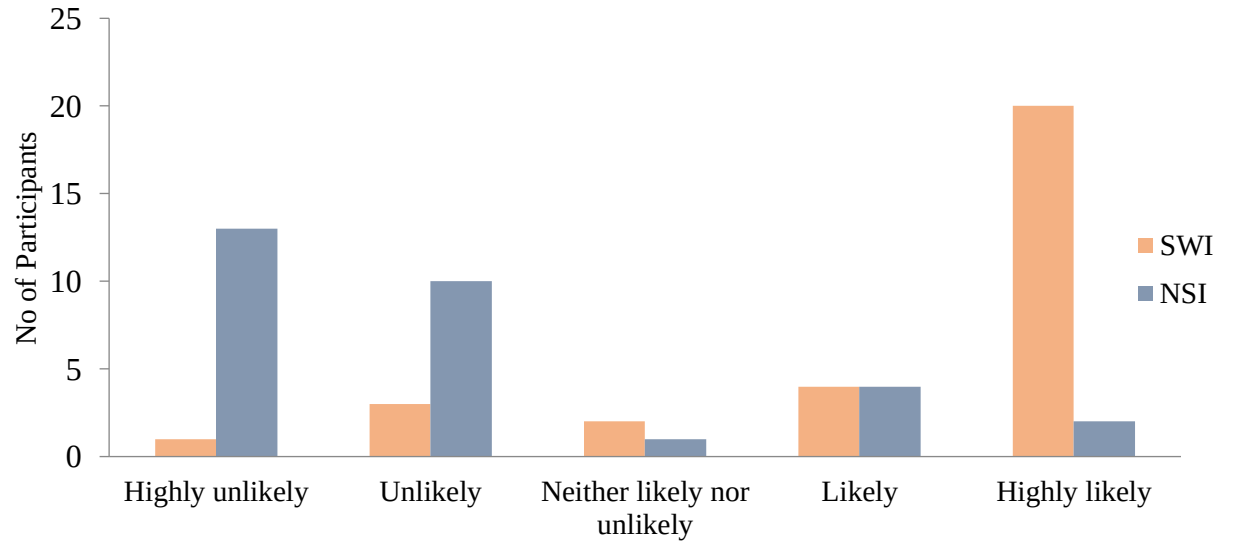

Figure 8: Likelihood of Reusing Method of Analgesia between Study Groups

More patients in the SWI group (73.3%) than in the normal saline group (13.3%) were more likely to recommend the mode of analgesia (P=0.001) (**Table 14**).

Table 14: Recommendation of Mode of Analgesia: N=60

		SWI	NSI	P
Would you recommend this method of Labour pain?	Strongly not recommend	0 (0.0)	13 (43.3)	n/a
	Not recommend	3 (10.0)	7 (23.3)	Ref.
	Neither recommend/not recommend	1 (3.3)	4 (13.3)	0.679
	Recommend	4 (13.3)	2 (6.7)	0.152
	Strongly recommend	22 (73.3)	4 (13.3)	**0.001**

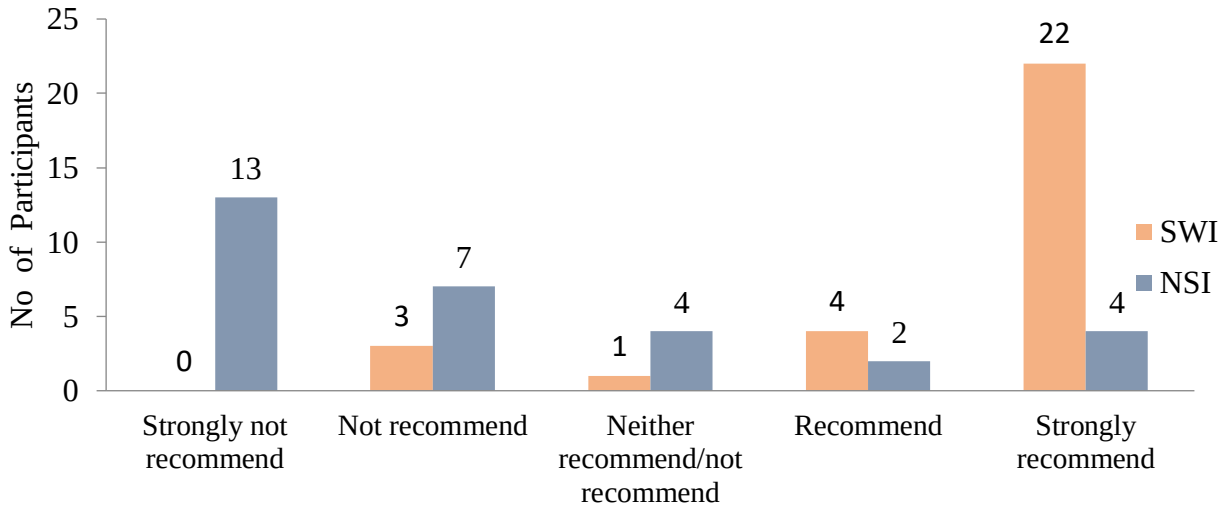

Figure 9: Probability of Recommendation of Mode of Analgesia between Study Groups

3.9 Mother to Baby Interaction

Mother to baby interaction was evaluated by measuring the duration from delivery to initiation of breastfeeding. Participants in the SWI group had a mean time of 65 minutes versus 122 minutes for NSI group, which was statistically lower (p<0.001) (**Table 15**).

Table 15: Mother to Baby Interaction

	SWI		NSI		
	M	SD	M	SD	P
Initiation of breastfeeding in min	55	39	122	42	<0.001

3.10 Adverse Drug Reactions

No adverse drug reactions were reported by participants in both groups. Women in the SWI did complain of more discomfort during administration of SWI than NSI, however this was expected as similar findings were reported in previous studies. Moreover, the discomfort was transient and lasted only 10-15 seconds.

CHAPTER FOUR

4 DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

4.1 Discussion

The data show that sterile water injections offered significantly more pain relief for continuous back pain during active phase of labour at 10, 30, 60, 90, and 120 minutes compared to normal saline injections. The effect was greatest at 120 minutes, with the mean difference of 49mm reported between the two groups (31). The participants in the SWI group reported less pain as labour progressed from time of injection up to duration of follow-up (120 minutes). The study showed that SWI offered pain relief for the entire duration of 120 min follow-up. This relates to SWI having an efficacy of equal to 120 minutes if not greater for continuous back pain relief in labour. More participants in the SWI group (23 to 25) who perceived a pain reduction of ≥30% compared to 3 to 4 in the NSI group. This was similar for those who perceived a pain reduction of ≥50%. The differences in pain perception of ≥30% and ≥50% were statistically significant.

Many studies in the developing world have reported similar results (9, 10, 37). Two RCTs, one carried by Farag in Egypt (9), the other by Rai in India, used the VAS to evaluate pain reduction at 10, 45 and 90 minutes and found a significant reduction in mean pain scores in the SWI group. Other studies which used alternative methods for pain assessment, Kushtagi and Bhanu (2009) (10) used Numerical Rating scale and Bahasadri *et al*. (2006) (37) used Face rating scale, also reported a significant pain reduction in the SWI group. A systematic review and meta-analysis carried out by Hutton *et al.* (2009) (6) reviewed eight RCT studies and found significant pain reduction in SWI group than NSI group at all time points.

The analgesic effect of SWI could be explained using the gate control theory of Melzack and Wall (3). Melzack and Wall's theory postulates that stimulus from non-nociceptive fibers can impair pain. This is because both nociceptive (pain) and non-nociceptive (non-painful) fibers synapse at the substantia gelatinosa and the transmission cells. They postulated the substantia gelatinosa is the gate in the spinal cord that controls transmission of sensory information from the primary afferent neurons to transmission cells in the spinal cord. This gating mechanism itself is modulated by the activity in the large and small fibers. Large-fiber activity inhibits (or closes) the gate, whereas small-fiber activity facilitates (or opens) the gate. Small fibers are the

A delta and C fibers while large fibers are the non-nociceptive fibers. (3) SWIs are salt-free. When administered, they cause osmotic stimulation and activate skin nociceptors and mechanoreceptors. The signals from the mechanoreceptors convey along large fibers, activate the gate control mechanism (substantia gelatinosa) and block the smaller fibers which carry signals from uterine contractions, thus inhibiting pain transmission to the dorsal horn. A second theory that could explain analgesic effect of SWI is that SWI stimulate the production of endogenous opioids, which proceed through descending pathways to the dorsal horn and inhibit the nociceptive transmission at the spinal level through a host of actions.

It is critical to evaluate the safety of SWI for use in labour pain relief for both the mother and the neonate. Several pharmacological agents have been shown to influence maternal outcomes or result in adverse drug reactions. Epidural analgesia is the most potent labour analgesia method. However, it has been linked with several maternal untoward effects. Epidural analgesia restricts maternal mobilization and may cause maternal hypotension and long-term backaches. Studies have also shown its association with increased rates of assisted delivery, which could be due to its relaxation effect on pelvic floor muscles (7). Opiods are a common alternative used to epidural analgesia. Just like epidural analgesia, opioids are also disadvantageous - they cause maternal side effects such as sedation, emesis respiratory depression and delayed gastric emptying. This study investigated the effects of SWI on the occurrence of adverse maternal outcomes. Compared to patients who received NSI, SWI did not influence the occurrence of adverse maternal outcomes. There was no statistical difference between number of participants who experienced postpartum hemorrhage, assisted delivery, admissions to HDU/ICU and maternal mortality between the two groups. Duration of second stage of labour was also not statistically different for the two groups (58 minutes for SWI versus 56 minutes for NSI group).

Similar findings have been recorded in multiple studies and meta-analysis (6, 8). Derry *et al*. (56) in 2012 did a retrospective review of studies. The analysis found no significance difference in the occurrence of adverse maternal outcomes between SWI and NSI groups, which was similar to what Hutton *et al.* (6) found in a meta-analysis in 2009. This corroborated with our findings. Moreover, no adverse drug reactions were reported by women in both study groups.

It is vital for any effective labour analgesics to have no untoward effects on the fetus and neonate, in addition to maternal adverse effects. Opiods have been found to induce adverse fetal and neonatal outcomes such as fetal bradycardia and neonatal respiratory depression amongst others. The study evaluated the effects of SWI on neonatal outcomes by measuring APGAR scores at 1, 5 and 10 minutes. Overall, the mean APGAR scores were identical for both groups: 9 at one minute, 9 at 5 minutes and 10 at 10 minutes. There were no neonatal mortalities within 24 hours of follow-up in both groups. These findings are similar to what Derry *et al*. (8) found in a retrospective review of studies. A study done by Genç Koyucu *et al*. in 2018 (57) also reported of no statistical difference in APGAR scores between SWI and NSI groups. These findings ascertain that SWI has no adverse effects on neonatal outcomes. Altogether, this affirms that SWI is a safe method of analgesia for use in first stage of labour.

Effects of SWI and NSI on mode of delivery were also evaluated as a secondary outcome. As discussed earlier, SWI did not influence rates of assisted deliveries. The incidence of caesarian deliveries was found to be lower in the SWI group compared to NSI group (1 versus 4) in our study. However, this was not statistically different ($p=0.161$). In contrast to these, Hutton *et al*. (6) in a systematic meta-analysis reported the SWI group to have significantly lower caesarian delivery rates. They recommended a large RCT to be done to evaluate the effects of SWI on the mode of delivery. Currently a multicenter trial (n-1866) is being done to further investigate this.

Early mother to child bonding is an important indicator of a positive birth experience for the mother. It instills feelings of joy of motherhood in mothers. Early interaction also increases the chances of establishing effective breastfeeding. Skin contact of mother to the baby, and baby suckling the mother's breast increases milk production. According to Deepika *et al*. (2018) (58) the timing of breastfeeding initiation does have an effect on neonatal morbidity and mortality. The mother's first milk, colostrum, is rich in immunoglobulins and nutrients. Observational studies have found that epidural analgesia causes a delay in alertness of babies and inhibits sucking of breasts, which often leads to delay in effective breastfeeding by babies (22, 23, 24). This study evaluated the duration taken by mothers in the SWI and NSI groups for initiation of breastfeeding. In the SWI group, the mean duration to initiation was 55 minutes, compared to 122 minutes in the NSI group, which was statistically significant ($p<0.001$). Mothers in the SWI took approximately half the duration before initiation of breastfeeding. This could be due to the

analgesic effects of SWI, which may lead to lower discomfort, less anxiety, emotional stability and general feeling of wellness in the immediate period after birth. This study shows that SWI does not affect mother to child interaction and initiation of breastfeeding. Furthermore, more studies should be conducted to investigate on the duration of breastfeeding initiation of SWI compared to other common pharmacological agents used in relief of labour pain.

The acceptability and satisfaction of SWI as a method of pain relief is also very essential. The study evaluated the acceptability of SWI among the African parturients. A 5-point Likert scale was used to evaluate the satisfaction of women with their method of labour analgesia, likelihood of using the same method for their subsequent delivery, and likelihood of recommending their method of analgesia to other women. Eighty seven percent (87%) of parturients in the SWI versus 13% in NSI group were either satisfied or very satisfied with their method of analgesia. Seventy three percent (73%) of parturients in the SWI versus 7% in NSI were highly likely to use their method of pain analgesia in their subsequent deliveries. Exceedingly more women in the SWI group than in NSI were likely to recommend their method of analgesia to other women (80% versus 3%). These differences were statistically significant. Our findings are comparable to those of Genç Koyucu (57), which found more women in the SWI were satisfied with their method of analgesia (85% vs 36%). A study done by Rai *et al*. in 2013 (40) reported that 83% of women in SWI group wanted to re-use their method of analgesia compared to 19% in NSI group. The high maternal satisfaction observed in the SWI group in our study and others could be linked with an effective analgesic property of SWI. The high number of women preferring to use SWI in their next delivery also attests to the acceptability of SWI within the African setting.

SWI is an effective, safe, and high acceptability intervention with many benefits. SWI is of a low cost than other pharmacological analgesics and require no special equipment for administration and storage. Neither special training nor highly qualified personnel is required for its administration. They are easily accessible in both remote and urban regions. These unique qualities of SWI make it a practical labour pain control method for developing countries, where many women are unable to cater for health care expenses (59). By soothing pain during labour, SWI can also improve the perception of women on delivery and make it an enjoyable experience. Women of developing countries and their experience. For many women giving birth is the most

distressful event of their life. SWI can leave a lasting impression at this moment, by improving the birthing experience of women (60).

4.2 Conclusions

- Sterile water injections is an effective method for pain management during active labour
- It does not influence the occurrence of adverse maternal outcomes and adverse neonatal outcomes, and is satisfactory for routine management of labour pain

4.3 Recommendations

- Sterile water injections should be considered for routine management of active labour
- Research studies that evaluate the efficacy of SWI injections for management of labour during the latent stage and second stage of labour are warranted

TIME LINES

Activity	Year							
	2018		2019					
	Nov	Dec	Jan	Feb	Mar	Apr	May	June
Presentation								
Ethics Review								
Training / Sensitization								
Data Collection								
Data Analysis & Report Writing								

BUDGET

Activity	**Cost (Kshs)**
Research Assistants	60000
Transport Costs	5000
Sterile water ampules (35)	3500
Normal saline ampules (35)	3500
Statistician	50000
Printing costs	15000
Training costs	20000
Contingencies (10%)	15700
TOTAL	**172700**

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APPENDICES

Appendix 1: Study Questionnaire

Effect of Subcutaneous Sterile water injections for relief of continuous back pain in labour at Kenyatta National Hospital. A randomized placebo controlled trial.

To be filled by midwife

Section 1.

1) U.I No.....
2) IP No.....

Biodata

3) Age (years) _____

4) Height (cm) _____

5) Weight (kg) _____

6) Marital status?
   - ☐Married
   - ☐Unmarried
   - ☐Separated/Divorced
   - ☐Widowed

7) Residence?
   - ☐Rural
   - ☐Urban

8) Level of education?
   - ☐No formal education
   - ☐Primary
   - ☐Secondary
   - ☐Tertiary

9) What is your occupation?
   - ☐Employed
     - If Yes:
     - ☐Formal
     - ☐Informal
   - ☐Unemployed

10) Parity _____

11) Gravidity - _____
12) Gestation by dates- ___wks ___days

Intrapartum assessment tool

13) Time at 1st injection administration _____
14) Cervical dilation(cm) at time of First injection administration _____
15) Need for oxytocin augmentation. ☐Yes ☐ No
16) Request for additional injections. ☐Yes ☐ No
- If yes, time at which administered. _____

17) Request for additional method of analgesia ☐Yes ☐ No

Birth outcome

18) Time at start of second stage of labour- _____
19) Mode of delivery
☐SVD
☐Vacuum
☐Caesarean Section

20) Time of delivery - _____
21) Maternal complications:
☐None
☐PPH
☐Retained placenta
☐HDU/ICU referral
☐Mortality

22) Apgar score
Reference score

Apgar Sign	**0**	**1**	**2**	Scores		
				1 m	5 m	10 m
Appearance (skin coloration	Bluish-grey or pale all over	Normal color all over (but hands and feet are blueish)	Normal color all over (hands and feet are pink)			
Pulse (Heart rate	Absent (no pulse)	Below 100 beats per minute	Normal (above 100 beats per m)			
Grimace (responsiveness or reflex irritability	Absent (no response to stimulation)	Facial movement only (grimace) with stimulation	Pulls away, sneezes, coughs, or cries with stimulation			

Activity (muscle tone)	No movement, floppy tone	Arms and legs flexed with little movement	Active spontaneous movement			
Breathing	Absent (no breathing)	Slow/ irregular breathing, weak cry	Normal rate and effort. good cry			
Total score						

23) Birth weight of baby (grams) - _____
24) Duration of 1st stage of labour _____hours____ minutes
25) Duration of 2nd stage of labour _____hours____ minutes

Breast Feeding
26) Time at initiation of breast feeding

Appendix 2: Pain Assessment Tool (VAS)

Effect of Subcutaneous Sterile Water Injections for Relief of Labour Pain at Kenyatta National Hospital. A Randomized Placebo Controlled Trial

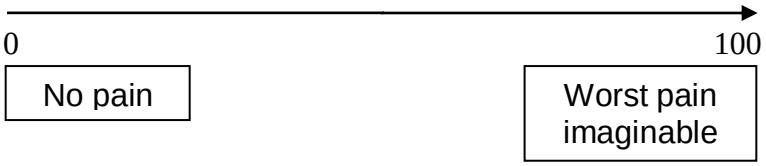
Pain Assessment Tool

(2.1) Unique Identification No.....

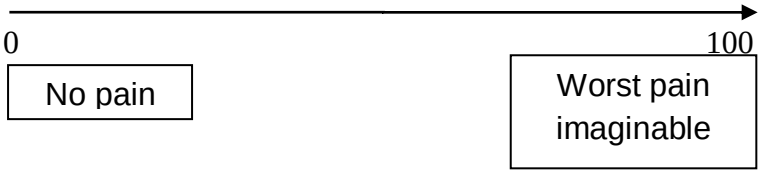
The section below is to be completed by the patient.

(2.2) Visual analogue scale

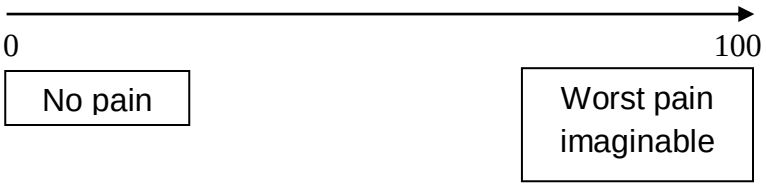
<u>At baseline</u>



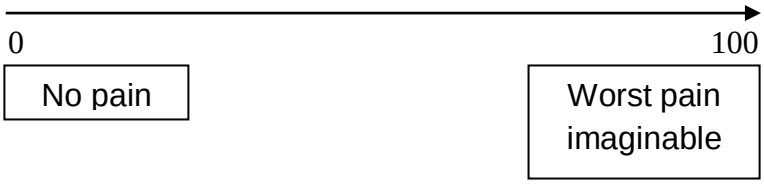
At 10 minutes post injection



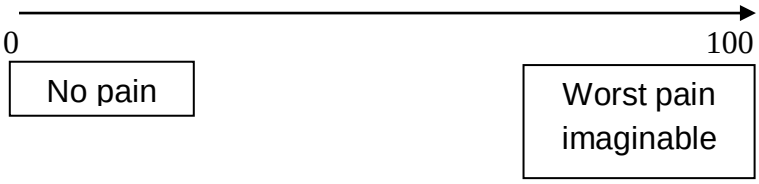
At 30 minutes post injection



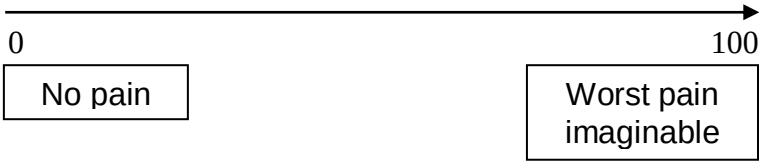
At 60 minutes post injection



At 90 minutes post injection



At 120 minutes post injection



Appendix 3: Satisfaction Assessment Tool

Effect of Subcutaneous Sterile Water Injections for Relief of Labour Pain at Kenyatta National Hospital. A Randomized Placebo Controlled Trial

Satisfaction Assessment tool

(3.1)Unique Identification No.....

The following questions below are to be completed by the patient
Please answer the following questions to give a feedback about your experience of labour pain relief with the method administered to you.

(3.2)How satisfied or unsatisfied are you with this method of Labour pain relief?

1. Very unsatisfied,
2. Unsatisfied,
3. Neither satisfied nor unsatisfied,
4. Satisfied
5. Very satisfied.

(3.3) how likely are you to use the same method of Labour pain relief in your future pregnancies?

1. Highly unlikely
2. Unlikely
3. Neither likely nor unlikely
4. Likely
5. Highly likely

(3.4) Would you recommend this method of Labour pain relief to other women?

1. Strongly not recommend
2. Not recommend
3. Neither recommend / not recommend
4. Recommend
5. Strongly recommend

Appendix 4: Informed Consent Explanation Sheet

Effect of Subcutaneous Sterile Water Injections for Relief of Labour Pain at Kenyatta National Hospital. A Randomized Placebo Controlled Trial

Informed Consent Form

Part A: Information

Introduction

My name is Dr Satbir Singh Karwal. I am a student, currently studying at University of Nairobi pursuing Master's Degree in Obstetrics and Gynecology. I am carrying out a study on the **Effect of Subcutaneous Sterile water injections vs normal saline injections for relief of labour pain**. This study is as part of my course work and university requirement for the completion of the course and award of the degree.

I will provide you with information about this study and welcome you to be part of this research. Your participation in this study is not compulsory. Before making your decision, you can consult with anyone you feel comfortable with about this study.

In case you do not understand some words, ask us to stop has we go through the information and we will take time to explain. If you have questions later, you can ask them of me, my research assistants or the hospital staff.

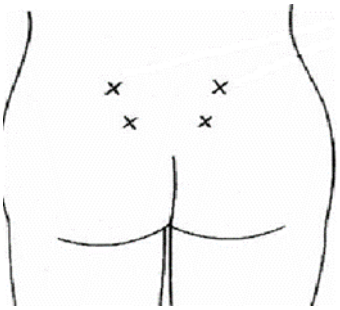
What is the purpose of this study?

Labour is a unique experience for every woman. Pain in labour can negatively affect the child birth experience. For women, labour may be their first instance of perceiving extreme pain. Several techniques have been used to relieve labour pain. Sterile water injections (SWI) is one of the methods used to relieve labour pain. This study is being carried to find out if SWI can reduce pain during labour and improve satisfaction of child bearing experience.

What are sterile water injections?

SWI is a technique that is used to provide relief from pain during labour. It is currently being used in several institutes globally. It involves injections of very small amounts of sterile water (0.5ml) under the skin at four points surrounding the lower back. This may cause a mild stinging sensation that may last for 20-30 seconds and disappear completely thereafter. To distract from the sting the injections are done during a contraction. As the stinging fades the labour pain eases, the pain relief may last for up to two hours. The injections can be repeated if needed.

SWI have been shown to provide good pain relief from back pain for most women (85 per cent). SWI have no known side effects and will not affect your baby. SWI can be used alongside any other form of natural or medical pain relief during labour.



Site of SWI administration

Type of Research Intervention

This research will involve administration of four injections on your lower back under the skin. This may cause a mild stinging sensation that may last for 20-30 seconds and disappear thereafter.

Who can participate in this research?

We are inviting all healthy pregnant women at a pregnancy of between 37 to 42 weeks, who expect to have a normal birth and experience severe labour pain.

Do you know your participation is not mandatory?

Your participation in this research is voluntary. It is your choice whether to participate or not. Do not feel pressurized in any way or by any person to take part in this study without your will.

What if you decide not to take part in this study?

If you decide not to take part in this study, you will still be entitled to receive all the routine services provided by the facility.

What if you change your mind during the participation period?

You are allowed to change your mind anytime during the participation period and withdraw from the study. You will still receive all the routine services provided by the facility.

What happens if I agree to enroll in study?

If you experience significant labour pain and are eligible to participate, you will be explained the study and clarification will be provided for any concerns you may have. You will be required to sign the consent form indicating that you have agreed to take part in the study.

You will then be randomly allocated to receive either SWI OR NSI. Your allocation to receive either will be by chance, like flipping a coin. The hospital staff and the study team will have no influence over which agent will be administered to you. The agent you have been allocated to,

will be administered by a mid-wife or research team member in the absence of the primary midwife that will care for you during your entire labour process. Your primary midwife will remain unaware of the agent used. Your midwife will ask you to rate your pain on a scale, a 100 mm line, before the SWI are performed, and again at 10 minutes and at 30 minute intervals after the procedure for a duration of 2 hours. We will also ask you to rate any discomfort you felt from the procedure itself.

After your baby's delivery, you will be asked a few questions about how satisfied you were with the pain relief method you were administered. The study will also gather data from your health record such as how long your labour was and what type of birth you had.

Alternative Intervention

As stated before, you will randomly be allocated to either SWI arm or NSI arm. NSI is the placebo group in this study. This means participants in this group will not receive SWI injections. NSI have been used in previous similar studies, and its use has not been observed to be related to any poor maternal and fetal outcomes. It has also not been associated with any adverse effects. NSI will be administered in a similar version to the SWI as explained before

Can I request for additional injections?

Yes, upon your request, you can receive one more additional set of injections.

Can I use other forms of pain relief as well?

Being a participant in this study does not mean you will not be able to use any other form of pain relief. You will be eligible to all other forms of labour pain relief methods of your choice whenever you wish so.

Risks

Apart from the brief stinging sensation during the procedure, there have been no adverse events reported during routine use of the procedure in previous studies using SWI.

Benefits

The study is not intended to directly benefit participants and if you agree to take part you will not benefit directly from the trial. However, you will assist in determining whether SWI are effective in providing pain relief for women with pain in labour.

Confidentiality

All aspects of the study, including all information and results, will be strictly confidential. Patients will be assigned a study number and only the study investigators will have access to participant's medical information. Any of your information will be accessed only by study staff with access to the files (they are protected by password).

The research team may only link your allocated study number to your identity if there is a risk of harm to you or others. No identifying information will be used during statistical analysis. Any presentations or publications emerging from this study will not contain any identifying information. You will not incur any additional costs as a result of participation in the study.

Will I be informed about the results when the research project is finished?
It is anticipated that the trial will run for 6 months. You will be able to request information about the overall progress of the project once it has concluded.

Who may I contact for further information or concerns?

You are free to discuss your participation in this study and ask any questions with the research assistants, hospital staff of KNH, the principal investigator Dr Satbir Singh Karwal (0721517831, drsatbirkarwal@gmail.com), and or any research supervisor. You should also feel free to contact the chairman of KNH/UON, the Research and Ethics committee, KNH Hospital, P.O. Box 20723-00202, Tel no 726300-9 Ext 44355, 44102 to share information or to raise any pressing concerns.

Appendix 5: Taarifa ya Idhini (Hati Cha Maelezo)

Effect of Subcutaneous Sterile Water Injections for Relief of Labour Pain at Kenyatta National Hospital. A Randomized Placebo Controlled Trial

Taarifa ya Idhini

Sehemu A: Taarifa

Kuanzishwa

Jina langu ni Dr Satbir Singh Karwal. Mimi ni mwanafunzi katika chuo kikuu cha Nairobi. Naisomea shahada ya Masters in Obstetrics and Gynecology. Ninafanya utafiti ju ya ***Effect of Subcutaneous Sterile water injections vs normal saline injections for relief of labour pain***. Hili utafiti ni sehemu moja ya kozi yangu ambalo ni lazima nifanye ili nihitimu na shahada.

Nitakupa taarifa kamilifu juu ya utafiti huu na umekaribishwa kuwa mmoja was washirika. Ushirika wako kwa hili utafiti sio wa kulazimishwa. Kabla ya kuamua kuwa mshirika was hili utafiti, umekubaliwa kuongea na kushauri yeyote unayemuamini juu ya hili utafiti.

Iwapo hautelewa maneno mengine, kuwa huru kutuuliza ili tuweze kukufafanua. Zaidi ya hayo, ukiwa na maswali zingine baadaye, kuwa huru kutuuliza. Watafiti wetu watakujibu kikamilifu.

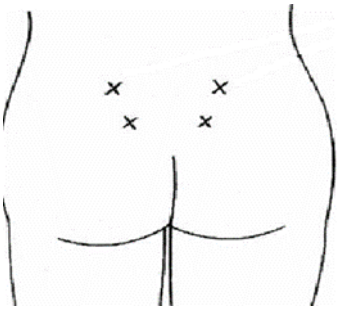
Kusudi wa hili utafiti ni nini?

Wanawake huwa na experience tofauti wakati wa kuzaa. Uchungu wa mimba inaweza kuathiri jinsi mtoto anavyozaliwa. Kuna mbinu nyingi za kupunguza unchungu was uzazi. Sterile water injections (SWI) ni moja ya hizo mbinu. Hili utafiti linashiria kuchunguza kama SWI zinaweza kupunguza unchungu wa uzazi na kuboresha uzalishaji wa watoto hapa Afrika.

Sterile water injections ni nini?

SWI ni mbinu ya kupunguza uchungu inayouhusishwa na kuzaa. Inatumika kwenye hospitali nyingi dunia nzima. Wakati wa kuzaa, wanawake hudungwa kiwango kidogo cha maji (0.5ml) kwenye sehemu nne ya mgongo. Wanawake wengine huhisi uchungu kidogo kwa sekunde 20-30. Ikitumiwa vizuri, SWI inaweza kupunguza uchungu wa uzazi kwa mda wa masaa mawili.

Kulingana na utafiti, wanawake asilimia 85 huhisi upungufu wa uchungu baada ya kutumia SWI. Zaidi ya hayo, SWI haina athari mbaya kwa wanawake na watoto na inaweza kutumiwa ns jinsi za kisasa au kiasili za kupunguza unchungu wa uzazi bila shida yoyote.



Eneo la kudungwa SWI

Matibabu za Utafiti

Wakati wa utafiti, washirika watadungwa sindano nne chini ya mgongo. Wakati wa kudungwa, utahisi unchungu kidogo kwa sekunde inshirini hadi thelathini hivi.

Nani anaweza kushiriki kwenye utafiti huu?

Tunakaribisha wanawake wajawazito (wiki 37 mpaka 42) walio na afya nzuri na wanatarajiwa kuhisi uchungu wanapaozaliswa kawaida.

Je, unajua kwamba kushiriki kwenye utafiti huu sio lazima?

Ushirika kwenye utafiti huu ni wa kujitolea. Ni uchaguzi wako kuwa mshiriki au la. Usihisi ya kwamba ni lazima ushiriki kwenye utafiti huu kama haujisikii.

Je, nikiubali kuwa mshiriki wa hili utafiti?

Ukiwa mshiriki wa utafiti, utapata huduma zote za kiafya unazostahili kwenye hospitali.

Je, nakubaliwa kubadilisha mawazao nikiwa mshiriki?

Umekubaliwa kubadilisha mawazo yako saa yoyote wakati was utafiti au kujiondoa kwenye utafiti. Hata hivyo, utaendelea kuhudumiwa ipasavyo kwenye hospitali.

Nini kinachotarajiwa baada ya kuwa mshirika?

Ukiwa na uchungu wa mimba na unstahiki kuwa mshirika wa huu utafiti, utaelezewa juu ye utafiti huu kikamilifu. Maswali yako yatajibiwa na wasiwasi zako kushugulikiwa kabla ya kuwa mshirika. Utahitajika kuweka ishara yako kwenye cheti chetu cha uhusika kuthibitisha ushiriki.

Baada ya kuthibitisha ushirika wako, utawekwa kewnye kikundi can SWI ama NSI. Kuwekwa kwenye vikundi itakua random. Wauguzi na watafiti hawatajua kikundi ambacho umewkewa au kuamua kikundi ambacho utawekewa. Mwisho, mkunga mwenye ujuzi atawadunga sindano na mtazamo wako wa uchungu kurekodiwa dakika 10, 30, 45, na 90 baada ya kudungwa sindano.

Baada ya kuzaa mtoto, utaulizwa maswali juu ya uridhishi wako na jinsi ya kupunuza uchungu ulichopokea. Takwimu kuhusu afya yako na ya mtoto pia zitarekodiwa.

Je, nawekza kuitisha sindano zaidi ya kiwango kinachopewa?

Ndiyo. Umekubaliwa kuitisha sindano zaidi wakati wowote.

Naweza tumia jinisi zingine za kupunuza unchungu?

Kuwa mhusika wa hili utafiti haimaanishi kuwa hauruhusiwi kutumia jinsi zinine za kupunuza uchungu. Madawa mbadala za kupunguza uchungu zitkuwepo wakati wa utafaiti huu.

Hatari

Kando na kusikia uchungu kidogo, hakuna tukio zingine mbaya zimeripotiwa kuhusu SWI.

Faida

Utafiti huu hautakufaidi moja kwa moja ukikubali kuwa mhusika. Hata hivyo, utasaidia kubaini kama SWI zina faida kwa wanawake wajawazito waliona maumivu ya uzazi.

Usiri

Mambo zote za hili utafiti, ikiwa ni pamoja na taarifa na matokeo zitakuwa siri. Wahusika watapewa nambari za uhusika na watafiti pekee ndiyo wataruhusiwa kusoma faili za hospitali. Hakuna pahali tutachapiza maelezo yako kwa hisiani ya utafiti huu. Hata watafiti hawatajua jina lako ama nambari yako ya kitambulisho. La mwisho, hautalipishwa kushiriki kwenye utafiti huu

Nitaarifiwa juu ya matokeo ya utafiti?

Utafiti huu inatarajiwa kuchukua miezi sita. Umekubaliwa kuitisha taarifa juu ya utafiti huu au matokeo yake baada ya kukamilishwa.

Naweza kuwasiliana na nani nikiwa na shaida?

Kuwa huru kuongea juu ya shida na au wasiwasi zako na watafiti, wauguzi katika hospitali kuu la Kenyatta, mtafiti mkuu, Dr Satbir Singh Karwal (0721517831, drsatbirkarwal@gmail.com), au msimamizi yeyote was utafiti huu. Pia, uwe huru kuwasiliana na mwenyekiti wa KNH/UON, the Research and Ethics committee, KNH Hospital, hupitia P.O.Box 20723-00202, au kupiga simu kwa nambari ya rununu, 726300 Ext- 44355,44102, ukiwa na shaida, taarifa, au maneno yanayokusumbua.

Appendix 6: Consent Participation Certificate

Effect of Subcutaneous Sterile Water Injections for Relief of Labour Pain at Kenyatta National Hospital. A Randomized Placebo Controlled Trial

Consent Participation Certificate

This research study is being conducted at the Kenyatta National Hospital and has been approved by the relevant Human Research Ethics Committees.

Student researcher: Dr. Satbir Singh Karwal

We are grateful for your consideration for participation in our study.
Please indicate with a tick (✓) that you agree with the following statements and sign the consent agreement below.

I ……

- ❑ Have read and understood the study participant explanation sheet;
- ❑ All my questions or queries have been answered to my satisfaction;
- ❑ Been informed of the possible risks or side effects of procedures being conducted;
- ❑ Understand that the project is for the purpose of research and that the project will involve randomization of participants;
- ❑ Been informed that the confidentiality of the information will be maintained and safeguarded;
- ❑ Give permission for access to my medical records, for the purpose of this research;
- ❑ Give permission to medical and health professionals, hospitals or laboratories outside this hospital, to release information concerning my disease and treatment which is needed for this trial and understand that such information will remain confidential;
- ❑ Been assured that I am free to withdraw at any time without comment or penalty;
- ❑ Agree to voluntarily participate in the project.

Signature: ...…….. Date: ……...

Witness: …… Date: ……...

Appendix 7: Cheti Cha Uhusirika

Effect of Subcutaneous Sterile Water Injections for Relief of Labour Pain at Kenyatta National Hospital. A Randomized Placebo Controlled Trial

Cheti Cha Uhusirika

Hi utafiti itafanywa katika hospitali kuu ya Kenyatta. Utafiti huu umesajiliwa na kuruhusiwa na wataalamu was utafiti zinzohusu binadamu.

Mtafiti: Dr. Satbir Singh Karwal

Tunafuria ushirika wako kwenye hili utafiti.
Tafadhali, onyesha au ashiria kwa alama ya (X) ya kwamba umekubaliana na taarifa hizi na kisha utie sahihi yako hapo chini.

Mimi ……

- ❑ Nimesoma na nikaelewa taarifa zote zilizo kwenye hati cha washirika.
- ❑ Mawsali yangu yote yamejibiwa kikamilfu
- ❑ Nimefafanuliwa uzuri na ubaya zinazoweza kutokana na vitendo vitakavyofanywa wakati wa utafiti huu.
- ❑ Nimeelewa ya kuwa huu ni utafiti na washirika watachaguliwa kwa nasibu.
- ❑ Nimeelezwa ya kwamba maneno yote yatakayoongelewa au kurekodiwa wakati wa utafiti huu utakua was siri. Taarifa zangu binafsi hazitawekwa huru.
- ❑ Nimepeana ruhusa kwa watafiti kuangalia rekodi zangu za hospitali kwa kusudi wa utafiti huu
- ❑ Nimepeana ruhusa kwa madaktari na watafiti wengine kweneye hospitali na maabara za kigeni kuangalia na kusoma taarifa zangu kwa ajili ya utafiti huu kwa siri.
- ❑ Nimearifiwa ya kuwa niko huru kujiondoa kwenye utafiti huu saa yoyote bila shida
- ❑ Nimekubali kwa hiari yangu kushiriki kwenye utafiti huu.

Sahihi: ...…….. Tarehe: ……...

Shahidi: …… Tarehe: ……...

Appendix 8: Adverse Event Reporting Form

EFFECT OF SUBCUTANEOUS STERILE WATER INJECTIONS VS NORMAL SALINE INJECTIONS FOR RELIEF OF CONTINUOUS BACK PAIN IN LABOUR AT KENYATTA NATIONAL HOSPITAL. A RANDOMISED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL

Adverse Event Reporting Form

Site Name…… Patient ID……

DIAGNOSIS……
…….....
.....

BRIEF DESCRIPTION OF REACTION
……
……
……
…….....

DRUGS ADMINISTERED PRIOR TO THE EVENT

Drug	*Dose*	*Route*	*Frequency*	*Date Started*	*Date Stopped*	*Indication*

Severity of Reaction	*Action Taken*	*Outcome*	*Causality of reaction*
☐Mild	☐Withdrawn	☐Recovering	☐Certain
☐Moderate	☐Increased	☐Recovered	☐Probable
☐Severe	☐Reduced	☐Hospitalised	☐Possible
☐Fatal	☐Dose changed	☐Need intervention	☐Unlikely
☐Unknown	☐Dose not changed	☐Unknown	
	☐Unknown		

Comments……
……
……
……

Reporting officer……. Date……
Email address…….. Phone……..
Title……. Signature……

.

Appendix 9: ERC Certificate

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/132

10th April, 2019

KENYATTA NATIONAL HOSPITAL APPROVED 10 APR 2019 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Dr. Satbir Singh Karwal
Reg. No.H58/80888/2015
Dept. of Obs/Gynae
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Karwal

Research proposal: Effect of subcutaneous sterile water injections vs normal saline injections for relief of continuous back pain in labor at Kenyatta National Hospital. A randomized, double blind, placebo controlled trial (P45/01/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above research proposal. The approval period is 10th April 2019 – 9th April 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

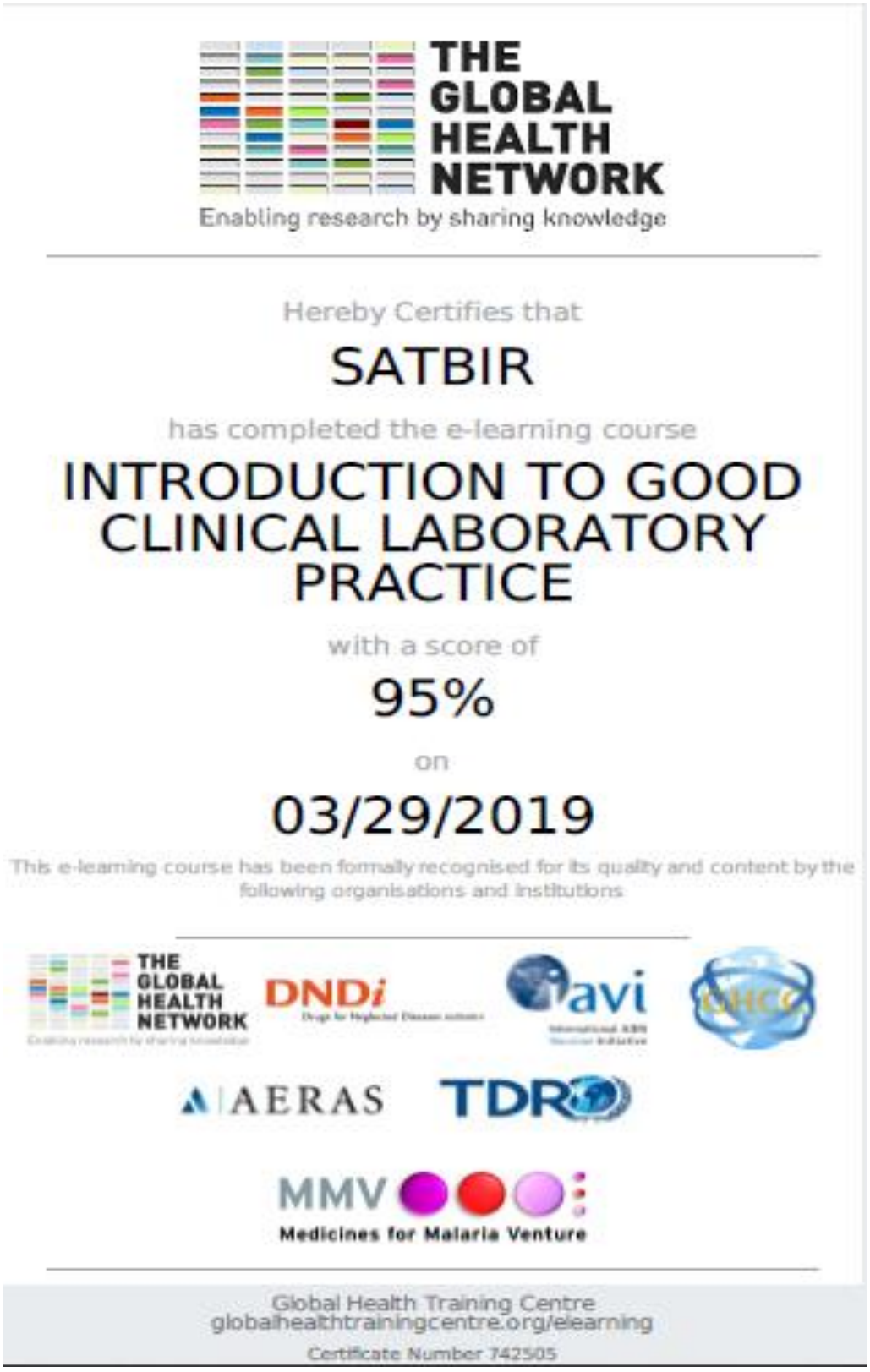
For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine,UON
The Chair, Dept. of Obs/Gynae, UoN
Supervisors: Dr. Alfred Osoti, Dr. Weston Khisa

Appendix 10: Good Clinical Practice Certificates



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Certificate Number 742505

NIDA Clinical Trials Network

Certificate of Completion

is hereby granted to

Satbir Karwal

to certify your completion of the six-hour required course on:

GOOD CLINICAL PRACTICE

MODULE:	STATUS:
Introduction	N/A
Institutional Review Boards	Passed
Informed Consent	Passed
Confidentiality & Privacy	Passed
Participant Safety & Adverse Events	Passed
Quality Assurance	Passed
The Research Protocol	Passed
Documentation & Record-Keeping	Passed
Research Misconduct	Passed
Roles & Responsibilities	Passed
Recruitment & Retention	Passed
Investigational New Drugs	Passed

Course Completion Date: 16 March 2018

CTN Expiration Date: 16 March 2021

Tracee Williams, Training Coordinator
NIDA Clinical Coordinating Center

Good Clinical Practice, Version 5, effective 03-Mar-2017

This training has been funded in whole or in part with Federal funds from the National Institute on Drug Abuse, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN272012010000024C.