Paracetamol versus Nalbuphine in Relieving Pain in the First Stage of Labour in Primigravida: A Double Blinded Randomized Controlled Trial

A Thesis

Submitted for partial fulfillment of Master degree in
Obstetrics and Gynecology

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2020

الباراسيتامول مقابل النالبوفين في تخفيف الألم في المرحلة الأولى من المخاض لدى السيدات البكريات (الحوامل للمرة الأولى): دراسة عشوائية ضابطة مزدوجة التعمية

رسالة

توطئة للحصول على درجة الماجستير
في **التوليد وأمراض النساء**

مقدمة من

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بكالوريوس الطب والجراحة ، ٢٠١١
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سورة المؤمنون – آية ٢٩

Acknowledgments

First and foremost, I feel always indebted to **Allah**, *the* ***Most Beneficent*** *and* ***Merciful*** *who gave me the strength to accomplish this work.*

My deepest gratitude to my supervisor, **Professor. Amr Abd El-Aziz Nadim,** *Professor of Obstetrics and Gynecology, Faculty of Medicine-Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision. May God bless him and keep him a sun lightening the way for the scientific students.*

I would like to express my great and deep appreciation and thanks to **Dr. Nermeen Ahmed Mostafa El Ghareeb,** *Lecturer of Obstetrics and Gynecology, Faculty of Medicine-Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work.*

Last but not least, I would also like to thank my colleagues, my patients and everyone helped me in this study.

✍ *Shimaa Hamdy Mohamed Eid*

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List of Abbreviations

Abbr.		Full-term
ACOG	:	American college of Obestricians and Gynecologists
BMI	:	Body mass index
CX	:	Cervix
NRS	:	5-numerical rating scale
NSAIDs	:	Non steroidal anti inflammatory drugs
PCIA	:	Patient – controlled intravenous opioid analgesia
PFS	:	Pain face scale
PGE	:	Prostaglandin
PV	:	Per vaginal examination
P value	:	Statistical Probability
SD	:	Standard deviation
SPSS	:	Statistical package for social science
TENS	:	Transcutaneous electrical nerve stimulation
VAS	:	Verbal rating scale and visual analogue scale

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Introduction

Labor is a physiologic process during which the fetus, membranes, umbilical cord, and placenta are expelled from the uterus ***(ACOG, 2016).***

First stage of labor begins with regular uterine contractions and ends with complete cervical dilatation at 10 cm. It is divided into a latent phase and an active phase. The latent phase begins with mild, irregular uterine contractions that soften and shorten the cervix. Contractions become progressively more rhythmic and stronger. The active phase usually begins at about 3-4 cm of cervical dilation and is characterized by rapid cervical dilation and descent of the presenting fetal part ***(Bataille et al., 2014; Hanley et al., 2016).***

Labour is generally considered to be a painful experience and analgesia is regularly required. In a study comparing different painful medical conditions, the average labour pain scores in primigravid and multigravid women where more than that of sciatic, dental or bone fracture pain scores. Stretch of the cervix during dilatation, ischaemia of the muscle wall of the uterus with buildup of lactate and stretch of the vagina and perineum in the second stage are the probable causes of labour pain ***(Abdollahi et al., 2014).***

Childbirth education, emotional support, massage, aroma therapy, audio-therapy, and therapeutic use of hot and cold have been promulgated as nonpharmacologic methods to relieve or mitigate the pain and suffering of childbirth. Techniques that require specialized training or equipment include hydrotherapy, intradermal water injections, biofeedback, transcutaneous electrical nerve stimulation (TENS), acupuncture or acupressure, and hypnosis. Most of these techniques have not been subject to rigorous scientific study; therefore, conclusions about their efficacy are not possible ***(Wong, 2009).***

Epidural analgesia is not a new technique in obstetric practice. It was first documented in the 19th century into obstetric practice ***(Silva and Halpern, 2010)*** but epidural analgesia for labor is a recent phenomenon. It is accepted that lumbar epidural analgesia is the most effective method of pain relief in labor, but its putative effects on labor and mode of delivery may influence clinical practice ***(Mousa et al., 2012).*** The method by which pain gets relief during labor includes regional, pudendal nerve blocks, epidural and systemic opioid analgesia. Intramuscular or intravenous opioids can provide an alternative in situations where regional analgesia is unavailable or contraindicated or if less invasive methods are preferred by the woman or obstetrician ***(Freeman et al., 2015).***

Systemic opioid analgesia is widely used around the world, although its use for labor analgesia lacks rigorous scientific study. There is a high incidence of maternal side effects, and at best, analgesia is incomplete. Existing data suggest that opioids provide little significant analgesia ***(Nelson and Eisenach, 2005).***

Although meperidine is the most commonly used systemic opioid, there are few studies comparing opioids and little scientific evidence that one opioid is better than another. All have similar, dose-related, maternal and fetal side effects. Maternal side effects include nausea, vomiting, dysphoria, delayed gastric emptying and respiratory depression. All opioids cross the placenta. *In utero* opioid exposure results in a slower fetal heart rate and decreased beat-to-beat variability ***(Drewes et al., 2013).*** The risk of neonatal respiratory depression depends on the dose and timing of maternal opioid administration. The active metabolite of meperidine, normeperidine, has a half-life of 60 hours in neonates ***(Wong et al., 2009).***

Theoretically, patient-controlled intravenous opioid analgesia (PCIA) has advantages compared to nurse- or midwife-administered opioid analgesia. These advantages include superior analgesia with smaller drug doses, resulting in a lower incidence of side effects, and patient control of analgesia. Studies of PCIA meperidine, nalbuphine, fentanyl,

and more recently, remifentanil, have been reported ***(McNicol et al., 2015).***

Nalbuphine Hydrochloride injection is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Nalbuphine Hydrochloride Injection can also be used as a supplement to balanced anesthesia, for preoperative and postoperative analgesia, and for obstetrical analgesia during labor and delivery ***(Kim et al., 2011).***

Nalbuphine Hydrochloride injection is a potent analgesic. Its analgesic potency is essentially equivalent to that of morphine on a milligram basis. Receptor studies show that Nalbuphine hydrochloride binds to mu, kappa, and delta receptors, but not to sigma receptors. Nalbuphine hydrochloride is primarily a kappa agonist/partial mu antagonist analgesic ***(van Niel et al., 2016).***

Although the exact mechanism of action is still a controversial issue, paracetamol (acetaminophen) is a safe and effective agent for pain management. Studies have suggested that paracetamol is an effective treatment for postoperative pain relief***. (Azam Foroughipour et al., 2011).***

Post-operative pain after Caesarean delivery, and perineal pain after child birth have proposed that paracetamol has an admirable analgesic effect. Based on our knowledge,

there are no significant clinical trials regarding paracetamol analgesic effect on labour pain in primigarvid women ***(Abdollahi et al., 2014).***

The onset of analgesia occurs rapidly within 5–10 minutes of intravenous paracetamol administration. The peak analgesic effect is obtained in 1 hour and its duration is approximately 4–6 hours. The antipyretic effects of intravenous paracetamol are also rapid with fever reduction occurring within 30 minutes of administration and lasting at least 6 hours ***(Chiam et al., 2015).***

Intravenous paracetamol is approved for the treatment of pain and fever in several countries worldwide. Intravenous paracetamol is administered as a 15-minute infusion. The recommended dosage in adults and adolescents weighing > 50 kg is 1 g up to four times per day, with a minimum interval of 4 hours between doses and a maximum daily dose of 4 g ***(Shahid et al., 2015).***

Aim of the Work

To compare between intravenous nalbuphine and paracetamol in relieving pain in first stage of labour in primigravida.

Labour Pains

The first stage of labour pains has been described as referred pain, this can be explained by the common neuronal pool supplying both the uterus and the anterior abdominal wall ***(Mc Donald, 2001)*** the results from dilatation of the cervix and lower uterine segment and from distension of the body of the uterus by uterine contractions and is transmitted by afferent nerve fibers (accompanied by sympathetic fibers) of the I0th, 11^{th} and 12^{th} thoracic and 1st lumbar nerves ***(Eltzschig et al., 2003 and Hawkins and Joy, 2010).***

The descending head causes pressure on the lumbosacral plexus responsible for pain felt in the back, thighs and legs **(Fig. 1)** ***(Hanley et al., 2016).***

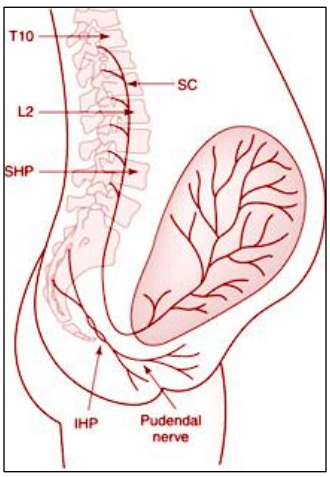

Figure (1): Peripheral nociceptive pathway involved in the pain of parturition ***(Dubin and Patapoutian, 2010).***