# Evaluation of intravenous infusion of Paracetamol in comparison with Meperidine as intrapartum analgesia in the first stage of labour

**Thesis**

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***By***

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# List of abbreviations

| | |
|---|---|
| **ACOG** | American College of Obstetricians andGynecologists. |
| **AUC** | A mean area under plasma concentration |
| **BMI** | Body mass index |
| **CGRP** | Calcitonin gene related peptide |
| **CI** | Confidence interval |
| **CNS** | Central nervous systeme |
| **CRF** | Case record form |
| **CSE** | Combined spinal epidural analgesia |
| **CVS** | Cardiovascular systeme |
| **DRG** | Dorsal root ganglia |
| **GCP** | Good clinical practice |
| **GIT** | Gastrointestinal tract |
| **HBB** | Hyoscine N-butylbromide |
| **HT** | Hydroxy tryptamine |
| **HTM** | High threshold mechanoreceptors |
| **IASP** | International association for study of pain |
| **LSCS** | Lower segment casarean section |
| **NAPQI** | N- acetyl-p-benzo-quinone |
| **NRM** | Nucleus raphe magnus |
| **NRS** | Numerical rating scale |
| **NS** | Non significant |
| **NVD** | Normal vaginal delivery |
| **PAC** | Patient controlled analgesia |
| **PAG** | Periaqueductal grey |

# List of abbreviations

| | |
|---|---|
| **PFC** | Pain face scale |
| **PGE٢** | Prostaglandin E٢ |
| **PMN** | Polymodal nociceptors |
| **S** | Significant |
| **SG** | Substantia gelatinosa |
| **SPSS** | Statistical package for the social science |
| **SRT** | Spinoreticular tract |
| **SSC** | Somatosensory cortex |
| **STT** | Spinothalamic tract |
| **TCM** | Traditional Chinese Medicine |
| **TENS** | Transcutenous electrical nerve stimulation |
| **VAS** | Visual analogue scale |
| **VRS** | Verbal rating scale |

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# *INTRODUCTION*

The most significant pain likely to be experienced by women is that associated with the child birth; uterine muscle hypoxia, lactic acidosis, distension of lower uterine segment, stretching of ligaments and pressure on bony pelvis may all contribute to the pain experienced in the first stage of labour ***(Creehan, 2008 )***. Analgesia is often required in labour for humanitarian and medical reasons. The American College of Obstetricians and Gynecologists ***(ACOG)*** and the American Society of Anesthesiologists issued a joint statement indicating that a woman's request for pain relief is a sufficient medical indication for pain relief ***(ACOG, 2002)***.

So adequate analgesia during labour has a positive influence on the course of labour ***(Keskin et al., 2003)***. Most women who deliver in modern obstetric units request some form of pharmacological and non pharmacological pain relief ***(Thurlow et al., 2002)***. The ideal obstetric analgesia should provide potent analgesic efficacy with minimal maternal and neonatal adverse effects, of all techniques of pain relief in labour, epidural analgesia is the most effective method, but it requires trained staff ***(O"Sullivan, 2005)***. Epidural analgesia appears to be effective in reducing pain during labour. However, women who use this form of pain relief are at increased risk of having an instrumental delivery. Epidural analgesia had no statistically significant impact on the risk of cesarean section, maternal satisfaction with pain relief and long-term backache and did not appear to have an immediate effect on neonatal status as determined by Apgar scores ***(Anim-Somuah et al., 2010).***

Pethidine (meperidine hydrochloride ) is the most commonly used opioids for analgesia, it is a simple and cheap drug in the management of labour pains, especially in developing nations where availability of facilities

is the main limiting factor for the use of more effective methods for the management of labour pains ***(Kamyabi et al., 2003).***

Studies on pethidine raised concern about its effects on the neoborn, this includes increased risk of fetal acidosis at birth, sleepy baby and less successful breast feeding. Some recent evidence suggests that babies whose mothers have pethidine in labour are more likely to develop dependence in later life ***(Sosa et al., 2006).*** Maternal side effects include CNS (dizziness, drowsiness, fatigue, headache, and sedation), GIT (nausea, vomiting, and constipation), CVS (orthostatic hypotension), respiratory depression and delayed gastric emptying ***(Tsui et al., 2004) .***

Paracetamol (acetaminophen) is a safe and effective analgesic administered orally or rectally ***(Bektas et al., 2009).*** At therapeutic doses, it is associated with fewer adverse effects than either opioids or nonsteroidal anti-inflammatory drugs ***(Hyllested et al., 2002).*** It is a very frequently used painkiller and antipyretic drug among pregnant women ***(Headley et al., ٢٠٠٤),*** as it crosses the placenta in its unconjugated form and is considered a drug without teratogenic effects ***(Rathmell et al., 1997).*** It is also well tolerated and has low incidence of gastrointestinal side effects. It has only weak anti-infla mmatory effects (***Boutaud et al., 2002).***

Perfalgan (IV paracetamol) provides onset of pain relief within ٥ to ١٠ minutes after start of administration. The peak analgesic effect is obtained in ١ hour and the duration of this effect is usually ٤ to ٦ hours. The maximal plasma concentration of paracetamol observed at the end of ١٥ minutes IV infusion of ٥٠٠ mg and ١g of perfalgan is about ١٥µg/ml and ٣٠µg/ml respectively ***(emc.medicines.org.uk, 2008)***.

# Aim of the work

## Primary objective:-

The the aim of this study is to compare the efficacy of intravenous infusion of paracetamol in comparison with meperidine (pethidine) in pregnant women undergoing labour, as demonstrated by the degree of pain relief during the labour process.

## Secondary objectives:-

١. To document safety and evaluate adverse events recorded during the study either maternal or fetal.

٢. To correlate with the duration of labour.

٣. Subsequent need of additional analgesia.

# *Pathophysiology of pain*

## Definition of pain:

The international association for study of pain (IASP), defined pain as : an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage ***(Merskey and Bogduk, 1994).***

## Nature of pain:

Pain is described as an unpleasant sensation associated with a specific part of the body ***(Melzak and Katz, 2006).*** It is produced by processes that either damage or are capable of damaging the tissues. Such damaging stimuli are called ‘‘noxious’’ and are detected by specific sensory receptors called ‘‘nociceptors’’ . These nociceptors are free nerve endings with cell bodies in the dorsal root ganglia (DRG) and terminate in the superficial layers of the dorsal horn of the spinal cord. Here, they relay messages by releasing neurotransmitters such as glutamate ***(Jeftinija et al., 1991).*** Substance P and calcitonin gene related peptide (CGRP***) (Lawson et al., ٢٠٠٢).*** These pain neurotransmitters will result in the activation of the second-order neuron via their corresponding receptor. The second-order neuron crosses the spinal cord to the contralateral side and travels up the spinothalamic tract (STT) until it reaches the thalamus. From there the third-order neuron is activated, traveling from the thalamus to the somatosensory cortex (SSC), which allows for the perception of pain ***(Lawson et al., 2002).***

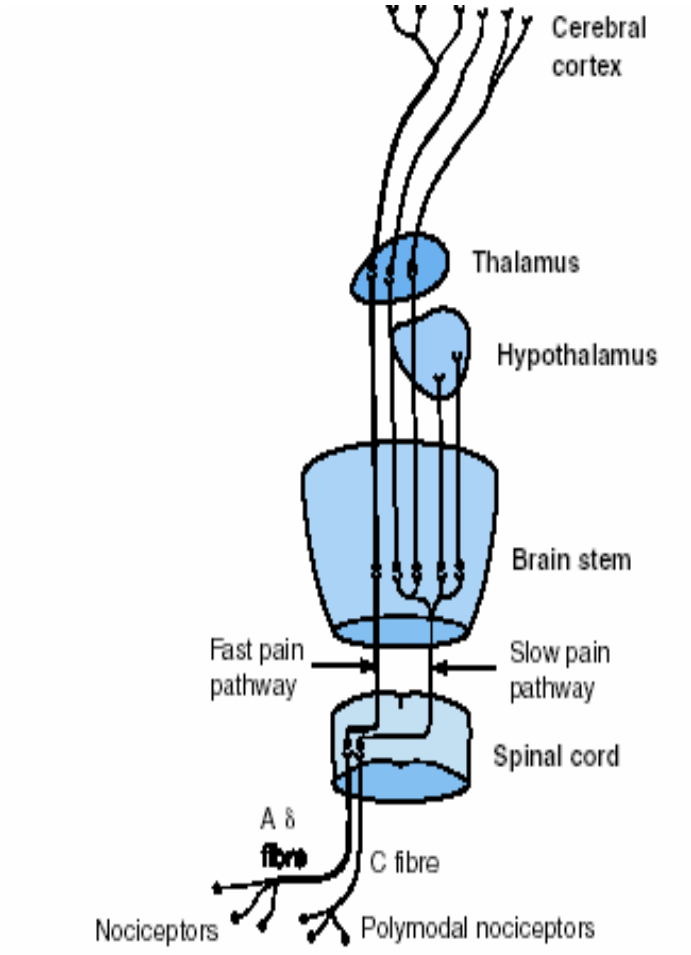


**Fig.(١):** Ascending tracts of spinal cord ***(Marchand, 2008).***

# Sources of pain:

١-**Nociceptive pain:** Results from damaged tissues.

- **Visceral pain.**
- **Somatic pain:** (Peripherally – Centrally).

٢-**Neuropathic pain:** Results from nerve damage or disease

***(Macintyre and Schug, 2007).***

# Types of pain:

## ١. Visceral pain:

Pain arising from viscera has a number of characteristic features:

• Poorly localized, associated with nausea and autonomic disturbance.

• May be colicky, often referred to another part of the body.

• Pain is elicited by distension, ischemia and inflammation.

Pain is mediated via A δ and C fibres, which travel with autonomic afferents that enter the spinal cord at the thoracic, upper lumbar and sacral segments. Because pathways are shared, activity in postsynaptic cells produced by visceral afferent activity is interpreted as arising from converging somatic afferents and pain may be referred to the corresponding somatic tissue ***(Catterine et al., 1998).***

## ٢. Somatic pain :

Sharp, stabbing pain and usually well localized to the area of injury. It results from injury of skin, mucosa, muscles, bone, tendons, arteries, ligaments and joints ***(McCaffrey et al., 2003)***

## ● Central nervous system and pain:

### ١. Primary afferent conduction:

Nociceptor terminations join to form axons whose cell bodies are in the dorsal root ganglia or trigeminal ganglion. The central terminations of these fibres are in the dorsal horn of the spinal cord ***(Catterine et al., 1998).***

## ٢. Dorsal horn of spinal cord:

The dorsal horns of the cord are divided into laminae on the basis of their histological appearances. Laminae ٢ and ٣ constitute the substantia gelatinosa (SG), where most of the modulation and sensory processing occurs **(*Dwarkanath, 1991*).** (Fig.٢)

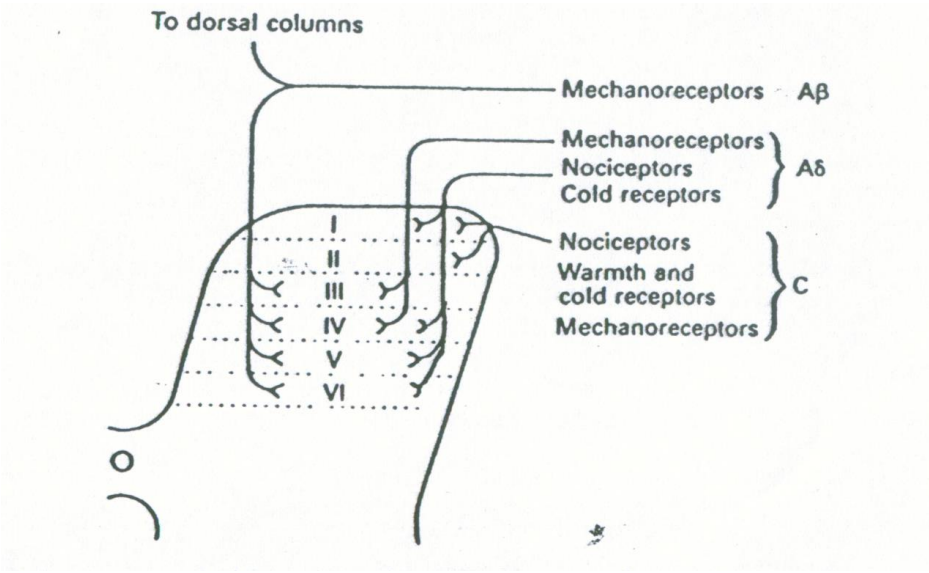


**Fig. (٢):** Schematic representation of the termination of the ٣ types of primary afferent neurons in the various layers of the dorsal horn of the spinal cord ***(Ganong, 1989).***

The impulses from spinal nerves reach the spinal cord via the dorsal spinal root (A-delta and C fibres), where they enter the region of the dorsal horn. Some of the sensory fibres pass directly through the dorsal horn and cross to the contralateral spinothalamic tract ***(Bonica, 1990).***

## ٣. Ascending tracts:

From the dorsal horn, nociceptor neurones ascend in the contralateral spinothalamic and spinoreticular tracts (SRT) in the anterolateral white

matter of the spinal cord. The spinothalamic tract sends collateral branches to the periaqueductal grey (PAG) matter in the midbrain. The system is well organized to provide discrete information ***(Catherine et al., 1998).***

The spinoreticular pathway ascends in the anterolateral cord and reaches the nuclei of the brain stem reticular formation, where they project to the thalamus, hypothalamus and thalamic intralaminar nuclei. These latter projects diffusely to the whole cerebral cortex. This system is involved in the perception of affective-motivational aspects of pain **(*Dwarkanath, 1991).***

### ٤. Descending modulation of pain:

Electrical stimulation of the midbrain PAG produces profound analgesia. The PAG receives input from the thalamus, hypothalamus, the cortex and collaterals from the spinothalamic tract and so is important center for descending control of pain ***(Woolf et al., 2004).***

## ● Pain gate theory:

The gate theory assumed that a noxious stimulus initiates an impulse in the peripheral nerve which ascends to the spinal cord, where it is modulated in the dorsal columns. The region in the dorsal column of this modulation was designated to be in the area of the substantia gelatinosa (SG) ***(Melzak and Wall, 2006).***