A STUDY ON ANALYSIS OF FETAL HEART RATE ABNORMALITIES COMPARING EPIDURAL ANALGESIA ROPIVACAINE 0.2% PLUS FENTANYL 2 µg/ML WITH BUPIVACAINE 0.1% PLUS FENTANYL 2 µg/ML DURING LABOUR

BY

DR MARY ANGELINE PETER

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LIST OF ABBREVIATIONS

AAG	Alpha 1-acid glycoprotein
BP	Blood pressure
bpm	Beats per minute
CTG	Cardiotocography
CNS	Central Nervous System
EFM	Electronic Foetal Monitoring
FHR	Foetal Heart Rate
LA	Local Anesthesia
LR	Labour Room
MAC	Minimum Alveolar Concentration
PCEA	Patient Controlled Epidural Analgesia

ABSTRAK

Tajuk: Kajian tentang kelainan analisa denyutan jantung janin membandingkan ubat tahan sakit epidural ropivacaine 0.2% ditambah fentanyl 2ug/ml dengan bupivacaine 0.1% ditambah fentanyl 2ug/ml semasa bersalin.

Latar Belakang dan Objektif: Ubat tahan sakit epidural melegakan rasa sakit bersalin secara efektif dan ramai ibu bersalin memilih teknik tersebut. Keselamatan janin dalam kandungan semasa bersalin penting dan kebanyakan pembiusan separuh badan sewaktu bersalin mempengaruhi denyutan jantung janin. Pelbagai kajian telah dilakukan untuk membandingkan kepekatan ubat bius setempat serta teknik pembiusan separuh yang berlainan untuk menganalisa kesan terhadap kadar denyutan jantung janin dan kesan terhadap cara melahirkan anak, kesan terhadap kestabilan ibu serta bayi. Jadi, kajian ini bertujuan untuk menganalisa kadar denyutan jantung semasa menggunakan dua kepekatan berlainan bagi ubat tahan sakit epidural dan kesan terhadap cara melahirkan bayi, kestabilan ibu serta keadaan bayi semasa lahir.

Keputusan: Berdasarkan cara melahirkan anak, ibu yang bersalin secara spontan bagi kumpulan yang menggunakan ropivacain adalah seramai 48 orang (71.6%) dengan bupivacaine pula adalah seramai 49 orang (83.1%). Bagi kelahiran melalui Caesarean pula kumpulan ropivacain adalah seramai 15 orang (22.4%) dan bagi bupivacaine pula ialah seramai 10 orang (16.9%). Perbandingan di antara kedua-dua kumpulan ubat bius setempat menunjukkan tiada

perbezaan yang bermakna dalam cara melahirkan anak. Seramai 115 ibu bersalin menunjukkan kadar denyutan jantung bayi yang normal di mana 96 orang (83.5%) dari mereka melahirkan secara spontan, 2 orang (1.7%) melahirkan secara instrumental dan selebihnya iaitu 17 orang (14.8%) menjalani pembedahan Caesarean. Dalam pada itu 11 ibu bersalin menunjukkan kadar denyutan jantung janin yang tidak normal, di mana 1 orang (9.1%) melahirkan secara spontan, 2 orang (18.2%) melahirkan secara instrumental dan seramai 8 orang (72.7%) secara pembedahan Caesarean. Ibu bersalin yang menunjukkan CTG yang tidak normal mempunyai peratusan yang lebih tinggi untuk bersalin secara pembedahan Caesarean. Seramai 27 ibu yang bersalin secara pembedahan Caesarean di mana seramai 18 orang menunjukkan CTG yang normal, 4 orang (22.2%) mengalami kelahiran tersekat, 2 orang (11.1%) mengalami kelemasan janin dan selebihnya 12 orang (66.7%) mengalami proses kelahiran yang lambat. Ibu yang menunjukkan CTG yang tidak normal, seramai seorang (11.1%) mengalami kelahiran tersekat manakala 8 orang (88.9%) mengalami kelemasan janin dengan nilai p=<0.001 yang bermakna. Tiada perbezaan bermakna dilihat dari segi kestabilan ibu serta bayi semasa lahir.

Kesimpulan: Berdasarkan kajian ini, ubat tahan sakit secara epidural sewaktu bersalin menggunakan ropivacain 0.2% dan bupivacain 0.1% dengan fentanyl 2ug/ml di dapati tidak memberikan perubahan dalam denyutan jantung janin. Terdapat peningkatan kadar pembedahan Caesarean disebab oleh CTG yang tidak normal dari kumpulan ropivacain diakibatkan kelemasan janin. Tiada perubahan dalam kestabilan ibu dan bayi yang dilahirkan.

ABSTRACT

Title: A study on analysis of foetal heart rate abnormalities comparing epidural analgesia ropivacaine 0.2% with fentanyl 2ug/ml to bupivacaine 0.1% with fentanyl 2ug/ml during labour.

Background and Objectives: Epidural analgesia effectively relieves labour pain and is widely chosen by parturients. Foetal well being is also important during labour as various neuraxial analgesia in labour is known to influence FHR tracings. Various studies focused on equipotent doses of local anesthetics and compared different techniques of labour analgesia in assessing foetal heart rate changes and its outcome on mode of delivery, effects on maternal haemodynamics and the neonatal outcome based on APGAR score. Therefore, this study was intended to analyze foetal heart rate changes using two different concentrations of epidural analgesia with opioids and its effect on the mode of delivery, maternal haemodynamics and neonatal outcome.

Methodology: A total of 126 patients were recruited in this prospective randomized cross sectional study. Maternal haemodynamics and foetal heart rate monitoring is documented 15 minutes before epidural administration and 15 minutes after epidural administration and subsequently every 30 minutes till four hours. CTG interpretation is documented. The observed outcome in this study were foetal heart rate abnormalities post epidural, maternal

haemodynamics before and after epidural analgesia in labour, mode of delivery and the neonatal APGAR score.

Result: Based on the mode of delivery between both the groups of epidural analgesia ropivacaine and bupivacaine, there were 48 (71.6%) in the ropivacaine group and 49 (83.1%) in the bupivacaine group who delivered spontaneously. 4 (6%) only delivered via instrumental in the ropivacaine group. Via caesarean section 15 (22.4%) in the ropivacaine group and 10 (16.9%) in the bupivacaine group. There were no significant changes in the mode of delivery between both the groups. 115 parturients had normal FHR, 96(83.5%) delivered spontaneously, 2 (1.7%) had instrumental delivery, 17 (14.8%) delivered via caesarean section. Whereas 11 patients had abnormal FHR, 1 (9.1%) delivered spontaneously, 2 (18.2%) via instrumental delivery and 8 (72.7%) via caesarean delivery. A higher percentage in caesarean delivery with abnormal CTG with a significant p value <0.001. Parturients for caesarean section were 27, 18 had normal CTG out of which 4 (22.2%) for secondary arrest, 2 (11.1%) for acute foetal distress, 12 (66.7%) for poor progress. 9 parturients had abnormal CTG, out of which 1 (11.1%) for secondary arrest, 8 (88.9%) for acute foetal distress with a significant p value=<0.001.There were no significant difference seen in maternal outcome and neonatal outcome.

Conclusion: This study revealed that with epidural analgesia in labour using ropivacaine 0.2% and bupivacaine 0.1% with fentanyl 2ug/ml, there were no foetal heart rate changes. There were increased risk for caesarean delivery with abnormal CTG in the ropivacaine group due to acute foetal distress. There were no changes in the maternal and neonatal outcome.

CHAPTER 1

INTRODUCTION

Foetal well being is the most important aspect during labour.To determine foetal well-being, one of the ways is by recording the foetal heart rate (FHR). Loss of beat to beat variability and deceleration patterns are known to be associated with foetal distress. Gynaecological factors, maternal and foetal factors, but also anaesthesiological factors can influence these FHR tracings. Decelerations and foetal bradycardia have been described after all types of effective labour analgesia such as (epidural,spinal,and combined spinal epidural(CSE) and intravenous opioids.(Nicole Maria Anna Adela Engel, 2011).

Epidural analgesia effectively relieves labour pain and is now widely chosen by parturients. In the US the use of neuraxial analgesia for labour increased to 77% in 2001 from 21% in 1981 and a little over 33% of parturients chose neuraxial analgesia for childbirth in UK from 2008-2009.(Cambic and Wong)2010. The additional use of opioids increases the effect of local anesthetic allowing the use of minimal concentration of local anesthetic, reducing the side effects such as hypotension and motor block. The minimum effective doses are used to avoid interference with the progression of labour and permit ambulation, however transient foetal heart rate(FHR) changes may occasionally follow with the use of any technique.(Capogna, 2001)

The beneficial effects of epidural analgesia may be offset by the detrimental effects such as prolonged labour, higher incidence of instrumental delivery and Caesarean section, maternal factor such as (hypotension,epidural haematoma and epidural abscess) and also towards the neonatal outcome. Although numerous studies have been done on the effects of epidural analgesia the results are contradictory.

(Cambic and Wong)2010 conducted a study and the evidence of neuraxial analgesia on labour outcome shows that neuraxial analgesia does not increase the risk of caesarean delivery .Conflicting evidence but overall it suggests increased rate of instrumental vaginal delivery in women receiving neuraxial labour analgesia.This was mainly affected by multiple factors, such as the degree of analgesia during second stage of labour, local anaesthetic concentration, method of epidural analgesia maintenance, technique and obstetric factors. There were no difference in the duration of first stage of labour and effective neuraxial analgesia increases the duration of second stage of labour.

A systemic review was done by (Leighton and Halpern, 2002) and their findings showed that parturients preferred epidural analgesia compared to parenteral opioids and they were more comfortable and satisfied,The length of first stage and second stage of labour were prolonged and the total incidence of instrumental delivery was higher in the epidural group. Neonatal outcome between the two groups showed no difference or more so favoured epidural analgesia. There were no significant trend toward an increase in the total number of caesarean delivery compared to the previous systemic review.(Halpern *et al.*, 1998).

In relation to dose related epidural analgesia there were numerous studies comparing bupivacaine and ropivacaine for labour analgesia. A randomized double blinded study by(Lee *et al.*, 2004) comparing epidural infusions of ropivacaine 0.1% with 2ug/ml of fentanyl with bupivacaine 0.1% with 2ug/ml Fentanyl focused on the obstetric outcome where the mode of delivery was similar between the two groups. Parturients who delivered vaginally, the duration of the first stage of labour was shorter in the ropivacaine group compared with the bupivacaine group. Incidence of maternal and neonatal outcome were similar between both the groups.

Another study was conducted by (Halpern and Walsh, 2003) which was a meta analysis also concluded that both ropivacaine and bupivacaine provided excellent labour analgesia and there is no significant difference between the two drugs with regards to neonatal, spontaneous vaginal delivery or any other obstetrical oucome. A randomized double blinded study(Fischer *et al.*, 2000) compared the administration of 0.1% ropivacaine and 0.5 ug/ml sufentanil with bupivacaine 0.1% and 0.5ug/ml sufentanil via a PCEA device. Outcome of this study produced effective pain relief in both the groups but maternal satisfaction was greater with the bupivacaine group. Ropivacaine drug was used more than bupivacaine during the second stage of labour, concluding that ropivacaine was less potent compared to bupivacaine and also due to the reduction in motor impairment.

Many studies were done on neuraxial analgesia in labour with different techniques, comparisons of equipotent concentrations of local anesthesia, comparisons with parenteral analgesia in labour with and without opioids and all these studies were

focused on the outcomes of maternal, neonatal and mode of delivery. There a few studies which has focused on the foetal wellbeing post neuraxial analgesia. A study on the incidence and clinical significance of foetal heart rate changes using intrathecal sufentanil or epidural bupivacaine for labour analgesia(Nielsen *et al.*, 1996),there were no significant difference in foetal heart rate between these two groups and also to the neonatal outcome.

A review on the effect of epidural analgesia on the foetal heart rate(Capogna, 2001) concluded that epidural or spinal analgesia in the absence of maternal hypotension or uterine hypotonus causes minimal changes in FHR. Even if there were it is transient and should not produce maternal or foetal morbidity. A recent French study (Korb *et al.*) analyzed foetal heart rate abnormalities occurring within one hour after laying of epidural analgesia using 0.1% levobupivacaine and sufentanil 0.2ug/ml. The results showed an increase in obstetric intervention in the abnormal foetal heart rate group and an absence of impact in the neonate state.

The importance of this study is to characterize abnormalities in the foetal heart rate by using two different concentration of epidural analgesia and its effect on the mode of delivery and neonatal outcome. The aim of this study is to characterize the abnormalities in FHR with ropivacaine 0.2%+ 2ug fentanyl and bupivacaine 0.1% + 2ug fentanyl, and its outcome on the mode of delivery and neonatal status. It attempts to address the potencies of different concentrations of the local anesthetic towards foetal heart rate abnormality during epidural analgesia in labour.

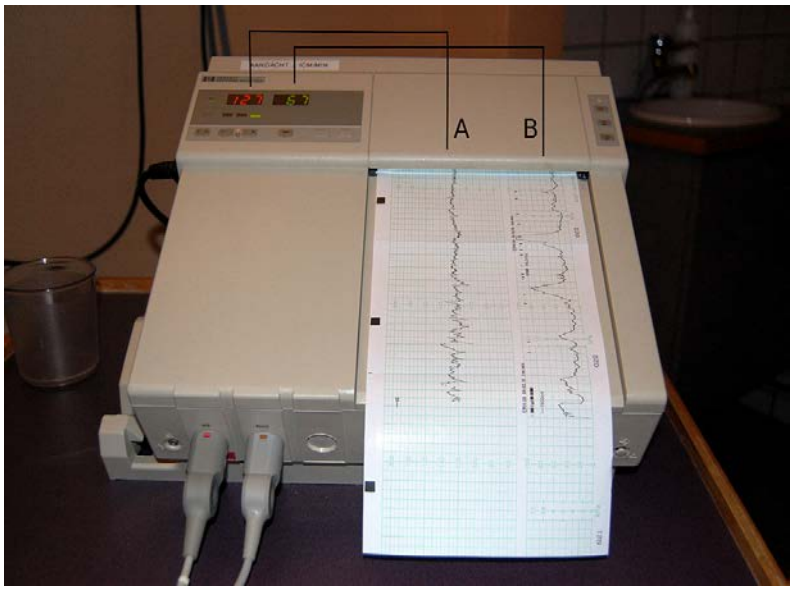
CHAPTER 2

LITERATURE REVIEW

2.1 Foetal Heart Rate

The foetal brain modulates the foetal heart rate through an interplay of sympathetic and parasympathetic forces. Foetal heart rate(FHR) monitoring can be used to determine if a foetus is well oxygenated. Despite the frequency of its use, limitations of EFM (electronic foetal monitoring) include poor interobserver and intraobserver reliability, uncertain efficacy and a high false positive rate. Foetal heart rate monitoring may be performed externally or internally. Most external monitors use a Doppler device with computerized logic to interpret and count the Doppler signals. Internal FHR monitoring is accomplished with a foetal electrode, which is a spiral wire placed directly on the foetal scalp or other presenting part.(Obstetricians and Gynecologists, 2009)

Figure 2.1 Cardiotochograph Machine



Foetal heart sounds were said to be first detected by Marsac in the 1600's. Killian proposed that foetal heart rate could be used to determine foetal well being in the 1600's. This thought went unnoticed until 1818 when Mayor and Kergaradec described the method of auscultating foetal heart sounds by placing the ear next to the maternal abdomen. Kergaradec also suggested that foetal heart sounds could be used to determine foetal life and multiple pregnancy and if it would be possible to assess foetal abnormalities from variations in the foetal heart rate. Evory Kennedy, an English physician, published guidelines for foetal distress and recommended auscultation of the foetal heart rate as a tool of intrapartum monitoring in 1833. By 1893, Von Winkel developed a criteria for foetal distress that remained unchanged until the arrival of electronic fetal monitoring.(Alfirevic *et al.,* 2006)

Since then, many methods of listening to the foetal heart have been developed and introduced into maternity care, with the goal of improving outcomes for neonates and easing the heartache for mothers and families when a baby dies or suffers long-term disability. For now, monitoring the foetal heart during labour, by one method or another, has become a routine part of care during labour, although access to such care are different across the world.(Alfirevic *et al.,* 2006)

2.2 Foetal Heart Rate Monitoring

Methods of monitoring the foetal heart rate

The foetal heart rate can be monitored either intermittently (at regular intervals during labour) or continuously (recording the foetal heart rate throughout labour, stopping only briefly, e.g. for visits to the toilet) as follows.

(1) Fetal stethoscope (Pinard) and hand-held Doppler

Intermittent monitoring can be undertaken either by listening to the foetal heart rate using a foetal stethoscope (Pinard) or a handheld Doppler ultrasound device and by palpating the mother's uterine contractions by hand. This is known as 'intermittent auscultation'.

Figure 2.2 Pinard's Stethoscope

Figure 2.3 Hand-held Doppler device

(2) Cardiotocograph (CTG)

Cardiotocograph electronically records the foetal heart rate and the mother's uterine contractions on a paper trace. **External CTG:** This is obtained by using a Doppler ultrasound transducer to monitor the foetal heart rate and a pressure transducer to monitor uterine contractions, both are connected to a recording machine. **Internal CTG:** Monitors the foetal heart rate with the CTG machine by attaching an electrode directly to the baby's presenting part usually its head. It is a form of continuous monitoring and requires a ruptured amniotic sac (either spontaneously or artificially) and a scalp electrode (clip) attached to the foetal head.(Alfirevic *et al.*, 2006).

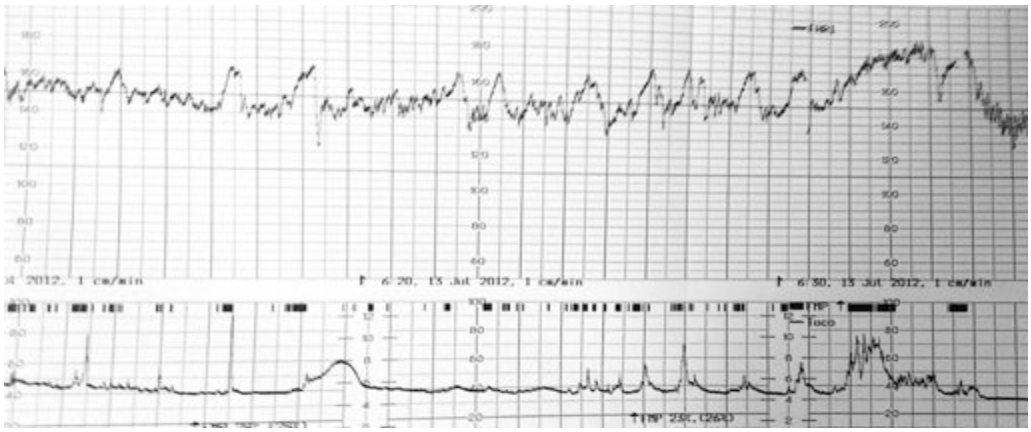
CTG monitoring and a systematic approach to CTG analysis may enable anaesthetists to better understand why obstetricians make specific clinical decisions. This understanding may aid communication and timely delivery especially when the foetus is considered at high risk.(ATOTW, 2013).Parturients receiving regional analgesia in labour, requires continuous electronic fetal monitoring for at least 30 minutes during establishment of regional analgesia and after administration of a further bolus of local anaesthetic agent. In most UK centres, continuous CTG monitoring is performed after the insertion of a labour epidural.(ATOTW,2013)

2.3 Baseline Fetal Heart Rate

The normal baseline foetal heart rate is defined as 110 – 160 bpm. Foetal bradycardia is a baseline rate of <110 bpm. Foetal tachycardia is a baseline rate of >160 bpm. Many foetal baseline bradycardias have no identifiable cause but may occur as a result of:

Cord compression and acute foetal hypoxia, post-maturity (> 40 weeks gestation) and congenital heart abnormality. Foetal tachycardia is associated with, excessive foetal movement or uterine stimulation, maternal stress or anxiety, maternal pyrexia, foetal infection, chronic hypoxia and prematurity (<32 weeks gestation)(ATOTW, 2013)

Figure 2.4 Normal CTG with the FHR upper and the tocogram below



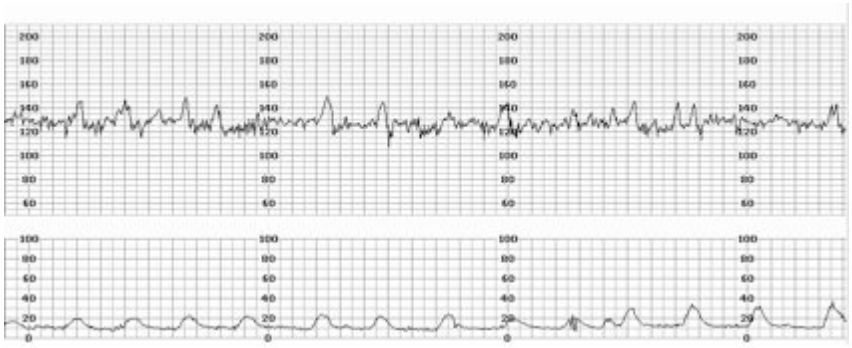
2.4 Foetal Heart Rate Variability

Variability refers to the normal beat to beat changes in FHR. Normal variability is between 5-15 bpm. Variability is measured by analyzing a one-minute portion of the CTG trace and assessing the difference between the highest and lowest rates during that period. Variability can be defined as: Normal 5-15 bpm , increased > 15 bpm , decreased <5 bpm, absent < 2 bpm. Foetal hypoxia causes absent, increased or decreased variability. Other causes of decreased variability include: normal foetal sleep-wake pattern, prematurity and following maternal administration of certain drugs including opioids. ATOTW,2013

2.5 Acceleration

Accelerations are periodic, temporary increases in FHR, characterized as an increase in FHR >15 bpm for more than 15 seconds. When accelerations are present, the CTG is reactive. Accelerations are associated with foetal activity and are considered as a sign that the foetus is healthy.

Figure 2.5 Foetal Heart Rate Acceleration



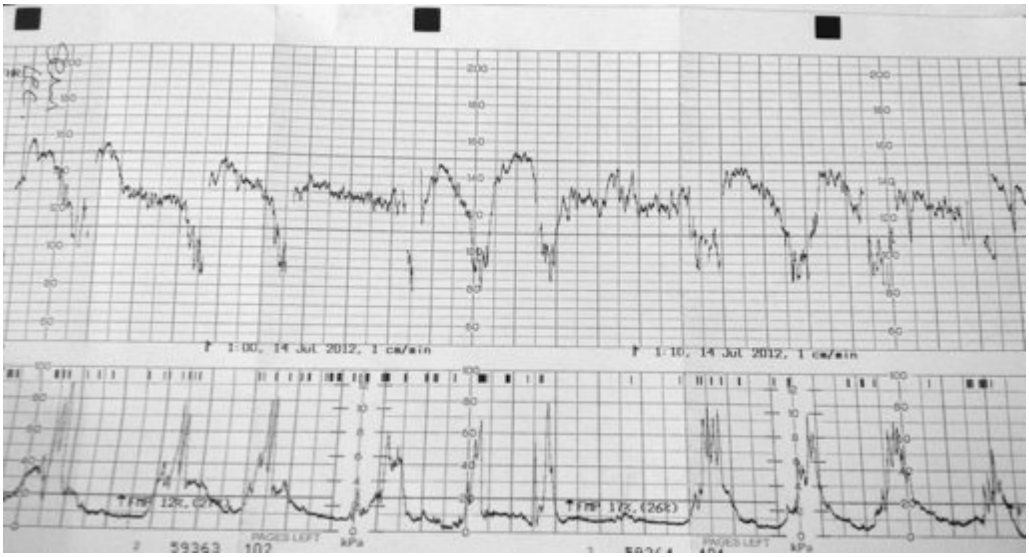
2.6 Deceleration

Decelerations are periodic, temporary decreases in FHR, and it's related to uterine contractions. They are categorized into four main types by their shape and timing in relation to uterine contractions. Uterine contractions must be monitored adequately in order for a deceleration to be correctly classified. Decelerations may be, early, late, variable and prolonged.

2.6.1 Early Deceleration

Early decelerations occur with each contraction and are uniform in shape. Early FHR decelerations appear as if reflecting the uterine contraction trace. The beginning of the deceleration occurs at the onset of the contraction and the baseline FHR recovers by the end of the contraction. The FHR usually does not fall by more than 40 bpm during an early deceleration. Compression of the foetal head during a contraction is the cause of early deceleration. These can be relieved by changing maternal posture and are a normal finding in the second stage of labour. They are not associated with a poor foetal outcome.

Figure 2.6 Foetal Heart Rate early deceleration

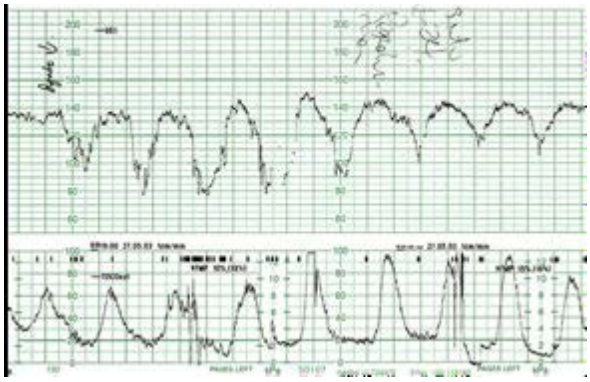


2.6.2 Late Deceleration

Late decelerations are uniform in shape on the CTG, but unlike early decelerations start after the peak of the uterine contraction. A deceleration in which the lowest point

occurs more than 15 seconds after the peak of the uterine contraction is defined as a late deceleration. They are usually associated with a reduction in the variability of the baseline FHR. Late decelerations are associated with decreased uterine blood flow and can occur as a result of: hypoxia, placental abruption, cord compression/prolapsed, increased uterine activity and maternal hypotension/hypovolaemia.ATOTW,2013

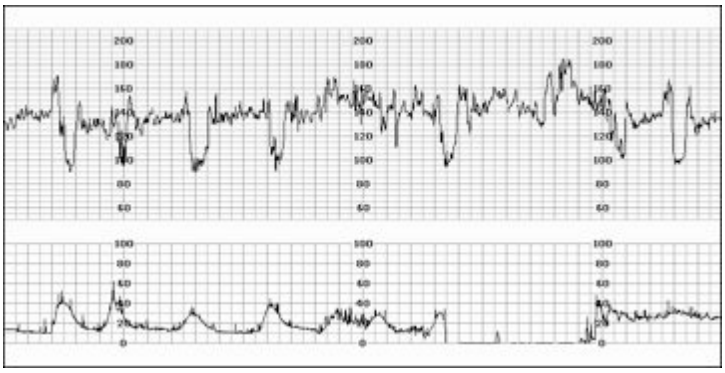
Figure 2.7 Foetal heart rate late deceleration



2.6.3 Variable Deceleration

Variable decelerations describe FHR decelerations that are both variable in timing and size. They may be accompanied by increased variability of the FHR. They are caused by compression of the umbilical cord and may reflect foetal hypoxia.

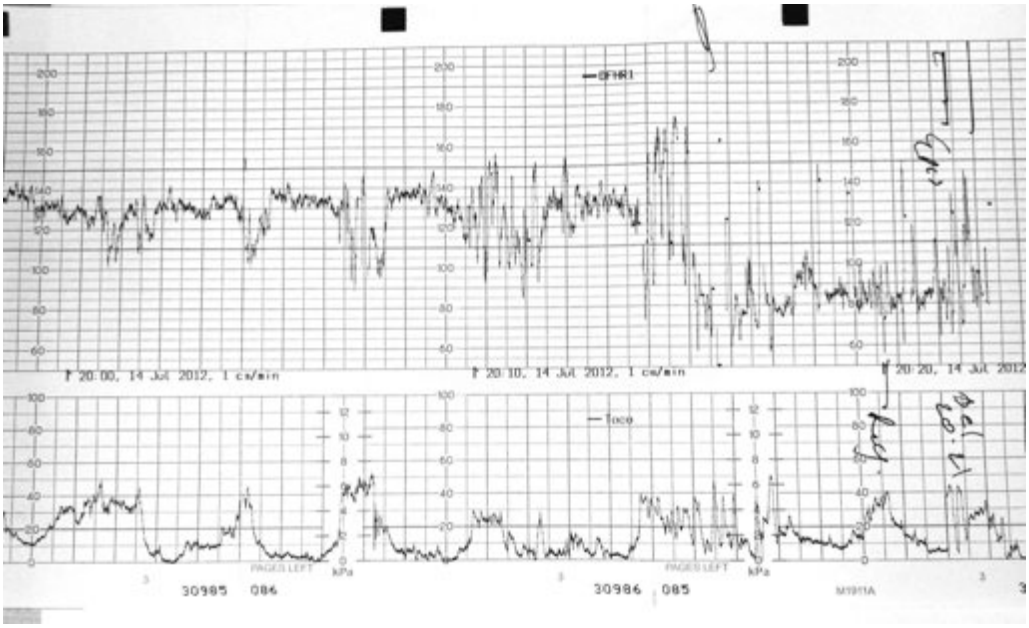
Figure 2.8 Foetal heart rate variable deceleration



2.6.4 Prolonged deceleration/bradycardia

A deceleration with a reduction in FHR of greater than 30 bpm that lasts for at least 2 minutes is termed a prolonged deceleration They are caused by a decrease in oxygen transfer to the foetus so can arise as a consequence of a wide variety of disorders including: maternal hypotension, umbilical cord compression and uterine hypertonia.(ATOTW,2013).

Figure 2.9 Foetal heart rate prolonged deceleration/bradycardia



2.7 Characteristics of CTG

A combination of several abnormalities increases the likelihood of foetal distress. Suspicious or abnormal features include: baseline FHR outside normal range of 110 – 160 bpm, baseline variability <5 bpm, reduced or absent accelerations and presence of decelerations.

2.8 Medications that effect the foetal heart rate

Foetal heart rate patterns can be influenced by the medications administered in the intrapartum period. These changes are transient, although they sometimes lead to obstetric interventions. Local anesthetic agents such as lidocaine and bupivacaine for epidural analgesia can lead to sympathetic blockade, maternal hypotension, transient uteroplacental insufficiency, and alterations in the FHR. Parenteral opioids also may affect the FHR.(Obstetricians and Gynecologists, 2009). A study comparing epidural analgesia with 0.25% of bupivacaine and intravenous meperidine reported that the variability was decreased, and FHR accelerations were significantly less common with parenteral analgesia compared with regional analgesia.(Hill *et al.,* 2003).A systematic review noted that there were no difference between those who did and those who did not receive epidural analgesia during labour in the rate of caesarean delivery for non reassuring FHR but this was associated with maternal hypotension or uterine hyperstimulation.(Lieberman and O'Donoghue, 2002).

Regarding combine spinal epidural analgesia in labour, there was a study conducted with 10ug of intrathecal sufentanyl with epidural bupivacaine and fentanyl or

intravenous meperidine(opioid). The results showed a significantly higher rate of bradycardia and caesarean delivery for abnormal FHR in the CSE group however the neonatal outcome were not significantly different between the two groups.(Gambling *et al.*, 1998).Another study comparing combine spinal analgesia with epidural analgesia, noted that FHR abnormalities were more common in the combine spinal epidural group.(Trial *et al.*)

There are also other drugs which can affect foetal heart rate such as butorphanol which causes a transient sinusoidal FHR pattern with a slight increased mean heart rate compared with meperidine.(HATJIS and MEIS, 1986). Cocaine causes decreased long term variability in the foetal heart rate.(Forman and Gandhi, 1991). Corticosteroids causes decrease in FHR variability and this happens with beta-methasone and not with dexamethasone. It causes abolishment of diurnal foetal rhythm and this effect usually occurs more than 29 weeks of gestation.(Rotmensch *et al.*, 1999). Magnesium sulphate causes a significant decrease in short term variability and it inhibits the increase in accelerations with advancing gestational age.(Hallak *et al.*, 1999). Terbutaline causes an increase in baseline FHR and incidence of foetal tachycardia.(Roth *et al.*, 1990).

There are other factors which causes changes in foetal heart rate such as maternal position as a cause of severe FHR changes after epidural bupivacaine labour analgesia. This is due to occult aortocaval compression.(Preston *et al.*, 1993). Maternal hypotension too has been associated to foetal bradycardia after epidural or spinal analgesia.Uterine hypertonus has been associated with foetal bradycardia after induction of labour analgesia such as CSE compared to epidural.(Landau *et al.*, 2009)

2.9 Labour Pain

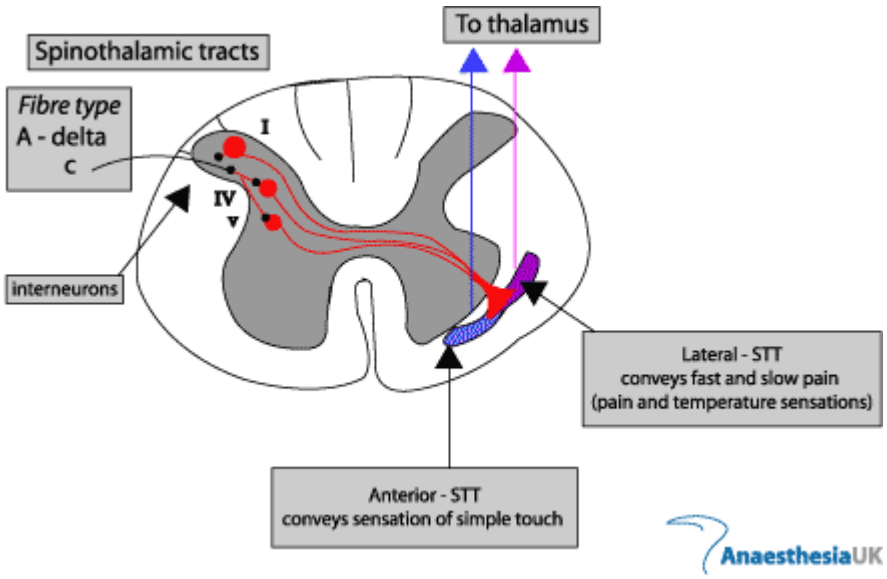
For most women labour causes severe pain, it is similar to that caused by complex regional pain syndrome. The American College of Obstetricians and Gynecologists and the American Society of Anesthesiologists (ASA) stated that, “There is no other circumstance where it is considered acceptable for an individual to experience untreated severe pain, amenable to safe intervention, while under a physician’s care.(Obstet Gynecol,2004). Without a medical contraindication, maternal request is a sufficient medical indication for pain relief during labour. Although severe pain is not life-threatening in healthy parturient women, it can have neuropsychological consequences. Postnatal depression may be more common when analgesia is not used.(Hiltunen *et al.*, 2004).And pain during labour has been correlated with the development of post-traumatic stress disorder.(Soet *et al.*, 2003).

2.9.1 Physiology of pain in labour

Labour pain is caused by uterine contractions and cervical dilatation and is transmitted through visceral afferent(sympathetic) nerves entering the spinal cord from T10 through L1. Later in labour, perineal stretching transmits painful stimuli through the pudendal nerve and sacral nerves S2 through S4. The maternal stress response can lead to increased release of corticotropin, cortisol, norepinephrine, β-endorphins, and epinephrine. Epinephrine can have relaxant effects on the uterus that may prolong labor.(Hawkins, 2010).

2.9.2 Acute Pain Pathway

Figure 2.10 Pain is transducted via small A delta and C afferent nociceptive fibres to the dorsal horn cell in the spinal cord.



Clinical pain is a result of either tissue injury (inflammatory) or nerve injury (neuropathic). When tissue injury occurs, a large number and variety of chemical mediators are liberated. These include hydrogen ions, noradrenaline, bradykinin, histamine, potassium ions, prostaglandins, purines, cytokines, 5-hydroxytryptamine, leukotrienes, nerve growth factor and neuropeptides. These substances in turn stimulate the small A delta and C afferent pain fibres.(Woolf and Chong, 1993). The terminals of small A delta and C afferent fibres act as receptors for nociception from superficial structures (skin and subcutaneous tissue), deep structures (muscle, fascia) and viscera.(Figure 2.10). These afferents pass within nerve fibres to the dorsal horn of the spinal cord where they either terminate superficially or pass more deeply into the dorsal horn laminae.(Rowlands and Permezel, 1998)

Action potentials generated within the dorsal cell neurone may participate in local spinal reflexes in which anterior and anterolateral horn cells stimulate skeletal muscle and sympathetic outflow. The action potential is also relayed centrally via the spinothalamic tract (Figure 2.11), from which the impulse is modulated successively by the reticular formation in the brainstem (integrative function), thalamus (level of arousal), hypothalamus and limbic systems (attention, mood and motivation). Nociception is modulated at the level of the dorsal horn by descending spinal tracts, which receive input from higher centres and the limbic system via stimulation of structures in the midbrain. This phenomenon is called 'stimulation-produced analgesia'. The type of nociceptive input appears to determine the descending tract stimulated and thus the neurotransmitter response.(Rowlands and Permezel, 1998).

Mechanical nociception activates the synthesis of β-endorphin which stimulates supraspinal opioid receptors and results in spinal release of enkephalins. Other endogenous opioids are known to be involved in the spinal modulation of nociception; proenkephalin is the precursor for met-enkephalin and other enkephalins which act by interaction with 'δ-opioid' receptors and dynorphin derived from prodynorphin interacts with 'κ-opioid' receptors.(Tseng *et al.*, 1995). Following the occupation of the opioid receptors on the dorsal horn neurones, the anti-nociceptive effect is produced by attenuation of the primary afferent nociceptive input, by inhibition of propagation of the action potential along the dorsal horn cell or by reducing the release of excitatory neurotransmitter substances from primary afferent terminals.

Figure 2.11 Ascending pathways

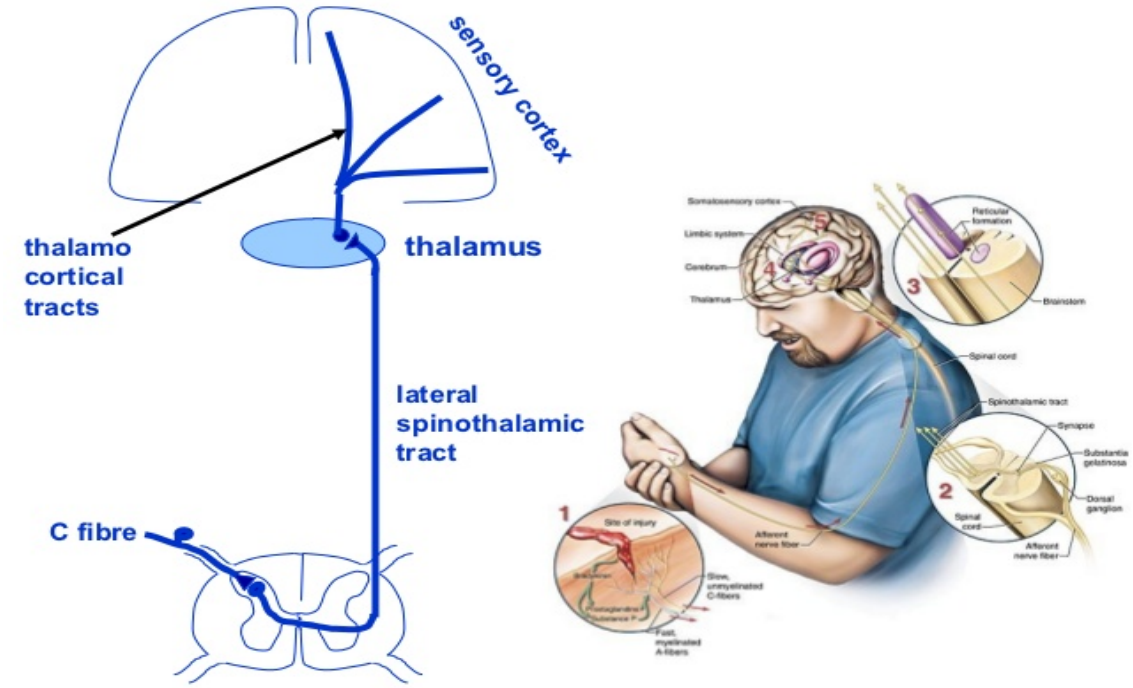
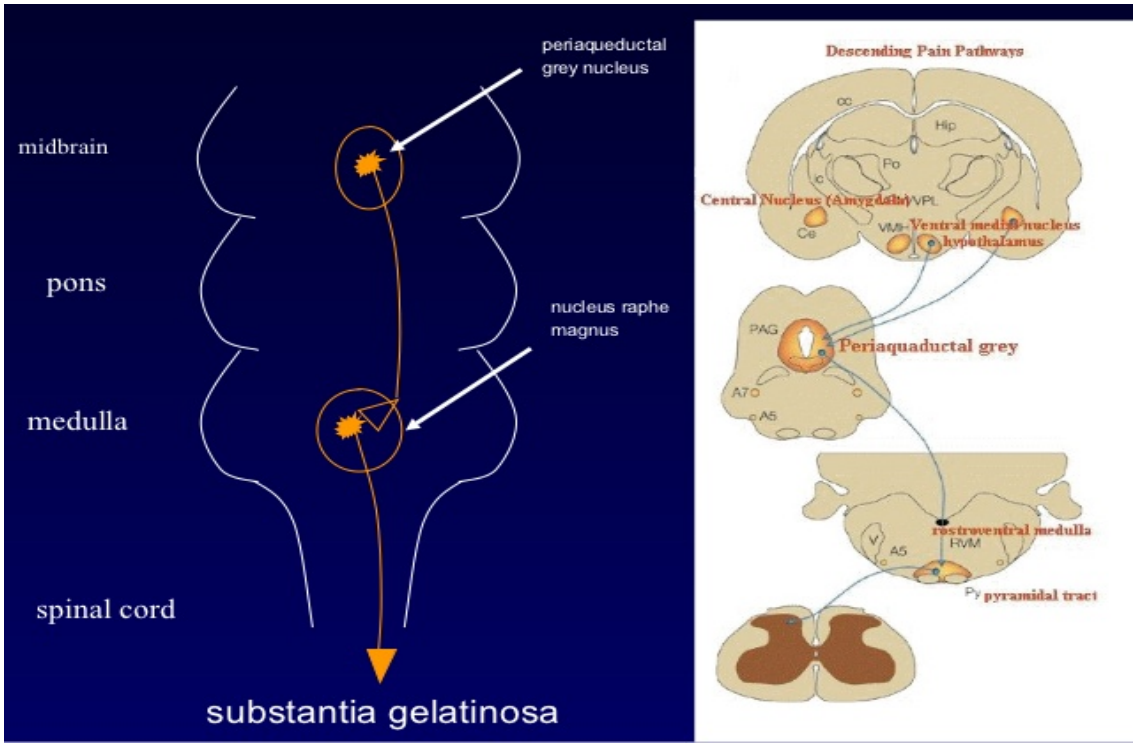


Figure 2.12 Descending pathway



2.9.3 Labour pain during first stage

The source of uterine nociception is not determined.During the first stage of labour, pain is predominantly mediated by mechanical distension of the lower uterine segment due to the mechanical dilatation of the cervix and the muscle contraction.The contraction of the uterus causes stretching and injury and thus causes the excitation of nociceptive afferents. During this stage a paracervical block with Bupivacaine has been shown to reduce pain significantly, proving that the cervix is an important source of pain at this time.(Ranta *et al.,* 1995).Strong contractions generated under isometric conditions in the presence of an abnormal fetal lie or slowly dilating cervix are frequently very painful. During labour, pain increases progressively due to the increase in duration and intensity of contractions.

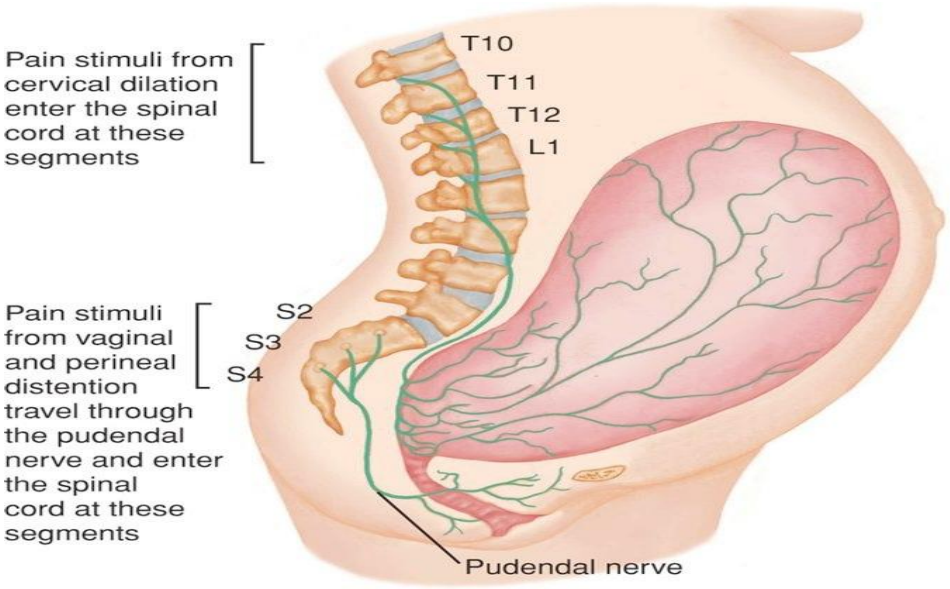
The uterus and cervix are supplied by afferents that accompany the sympathetic nerves in the uterine and cervical plexus, the inferior hypogastric plexus, the superior hypogastric plexus and the aortic plexus.(Figure 2.5).Pain is transmitted via small unmyelinated slow conducting C visceral fibres.They pass through the lumbar and lower thoracic sympathetic chain to the posterior nerve roots of the 10^{th},11^{th} and 12^{th} thoracic and 1^{st} lumbar nerves to make synaptic contact with the interneurones in the dorsal horn. Bradykinin, leukotrienes ,serotonin, substance P, prostaglandins and lactic acid are the chemical mediators that cause the excitation of these fibres.(Rowlands and Permezel, 1998).Contraction pain is transmitted slowly and its poorly localized. It is referred to the dermatomes supplied by T10, T11,T12 and L1.During the early first stage its felt as a dull ache over the area supplied by T11and T12. As the labour

progresses, pain increases and becomes more severe and is referred to the abdomen, lower lumbar and upper sacrum supplied by T10 and L1.

2.9.4 Labour pain during second stage

Distension of the lower segment and cervix continues to cause pain with similar distribution at, the first stage.In the second stage, increasing pressure is exerted by the presenting part within the pelvis. Pain at this stage is usually described as sharp and localized to the perineum, anus and rectum but also felt in the thighs or legs.This is due to the traction and pressure on the parietal peritoneum, uterine ligaments, urethra, bladder, rectum, lumbosacral plexus, fascia and muscles of the pelvic floor. Due to the direct pressure of the presenting part on the lumbosacral plexus, neuropathic pain occurs.Pudendal nerve arising from the S2, S3 and S4 via fine myelinated rapidly transmitting A delta fibres is stimulated as the vagina and perineum is stretched.Impulses pass to the dorsal horn cell and then via the spinothalamic tract to the brain.(Rowlands and Permezel, 1998)

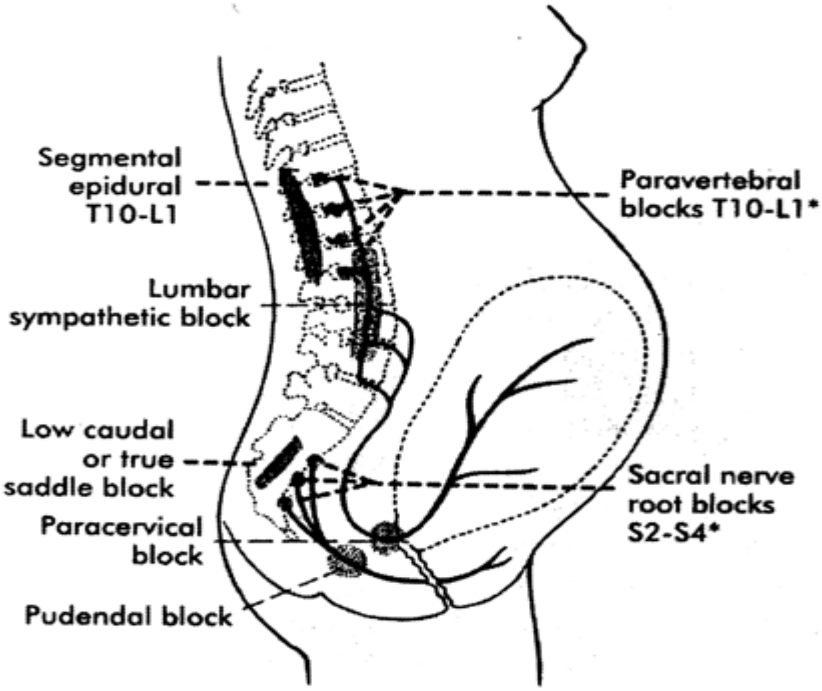
Figure 2.13 Neural pathway in labour



Segmental and suprasegmental reflex responses from the pain of labour may effect respiratory, cardiovascular, gastrointestinal, urinary and neuroendocrine function.These responses are mediated by pain and its evidenced by the fact that they can be prevented or abolished by central neural blockade.(Rowlands and Permezel, 1998).

2.10.1 Neuraxial analgesia in labour

Figure 2.14. Various neuraxial analgesia in labour

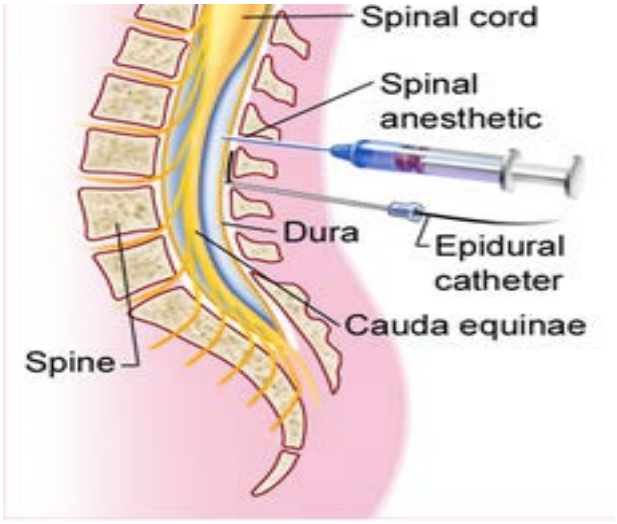


There are various methods of neuraxial analgesia in labour as shown in the above diagram,(Lumbar epidural, combine-spinal epidural, paravertebral block, lumbar sympathetic block, saddle block, paracervical block, pudendal block and sacral nerve roots block). The focus of the study is based on lumbar epidural analgesia in labour. Epidural analgesia for labor and delivery involves the injection of a local anesthetic agent (e.g.,lidocaine or bupivacaine) and an opioid analgesic agent (e.g., morphine or fentanyl) into the lumbar epidural space (Fig 2.15). The injected agent gradually

diffuses across the dura into the subarachnoid space, where it acts primarily on the spinal nerve roots and to a lesser degree on the spinal cord and paravertebral nerves. In spinal analgesia, which is often combined with epidural analgesia, the analgesic agent is injected directly into the subarachnoid space, resulting in a more rapid onset of effect. Successful epidural analgesia produces a segmental sympathetic and sensory nerve block and a decrease in endogenous catecholamines with the onset of pain relief.(Abboud *et al.*, 1983).Hypotension or normalization of blood pressure to prelabour levels may occur with vasodilatation, which may result from sympathetic nerve blockade and a decrease in circulating catecholamines. Other side effects are FHR abnormalities and prolonged second stage of labour.

Advantages of epidural analgesia in labour is its effective, with the addition of opioids to the reduced dose of local anesthetics causes faster onset of analgesia, due to the lower dose there is lesser motor blockade and allows parturients to ambulate.

Figure 2.15 Epidural analgesia and combined spinal-epidural analgesia



2.10.2 Anatomy of the Lumbar Spine

The lumbar vertebra has a larger kidney-shaped body and its vertebral foramen is larger than that of the thoracic vertebra. Its transverse processes are long and slender and its articular processes are directed (superior) posteromedially and (inferior) anterolaterally. Its spinous process is shorter, broader and more horizontal than those of the thoracic vertebrae.The articular surfaces of the bodies of adjacent vertebrae are covered by hyaline cartilage and united by a thick fibrocartilaginous intervertebral disc. These are strong cartilaginous joints designed for weight-bearing. The disc is a shock absorber, its centre, the nucleus pulposus, is gelatinous and surrounded by a fibrous part, the annulus fibrosus. Adjacent vertebrae articulate by two synovial facet joints between the paired articular processes.(AnesthesiaUK,2004)

Figure 2.16 Anatomy of the lumbar vertebra