EVALUATION OF POST-CAESAREAN PAIN MANAGEMENT, PAIN INTENSITY AND RISK FACTOR AMONG PATIENTS IN HOSPITAL PULAU PINANG

by

HANAN HUSSEIN JASIM

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In the name of Allah the most gracious the merciful. First and foremost, Praise be to Allah, Lord of the worlds; and prayers and peace be upon the master of messengers, the Prophet Mohammed (PBUH), our leader in this life until "the end".

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TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

LIST OF ABBREVIATIONS

APS	Acute pain service
BC	Before Centaury
BMI	Body mass index
CS	Caesarean section
CGPR	Calcitonin gene related peptide
CNS	Central Nervous System
CPD	Cephalopelvic disproportion
CRC	Clinical Research Center
DRG	Dorsal root ganglion
EA	Epidural Anaesthesia
FDA	Food and Drug Administration
GA	General Anaesthesia
HIV	Human immunodeficiency virus
HPP	Hospital Pulau Pinang
IASP	International assassination for the study of pain
IM	Intramuscular
IT	Intrathecal
IV	Intravenous
JCAHO	Joint Commission on Accreditation of Healthcare Organization
NA	Neuroxial Anaesthesia
NPI	Numeric pain Intensity scale

NRS	Numeric rating scale
NSAID	Non-steroidal Anti Inflammatory Drug
OR	Odds ratio
PCA	Patient control analgesia
SA	Spinal Anaesthesia
SD	Standard deviation
SSI	Surgical site infection
UK	United kingdom
USA	United States of America
USM	Universiti Sains Malaysia
UTI	Urinary tract infection
VAS	Visual analogue scale
VD	Vaginal delivery
VDS	Verbal descriptor scale
WHO	World Health Organization

PENILAIAN PENGURUSAN KESAKITAN, INTENSITI KESAKITAN DAN FAKTOR RISIKO PASCA CAESAREAN DALAM KALANGAN PESAKIT DI HOSPITAL PULAU PINANG

ABSTRAK

Sejak beberapa tahun kebelakangan ini, kadar pembedahan semasa bersalin (caesarean section, CS) meningkat secara signifikan, iaitu 15 - 25% daripada kelahiran. Dalam tempoh pasca-CS, iaitu daripada sakit yang sederhana hingga sakit yang teruk selepas pembedahan, adalah masalah yang biasa dilaporkan. Analgesia pasca-CS yang baik mampu meningkatkan kebolehan fungsi maternal dan interaksi dengan bayi yang baru lahir. Terdapat beberapa pilihan analgesia untuk mengoptimumkan pengurusan sakit, yang setiap satunya mempunyai keberkesanan dan keselamatan yang berbeza. Kajian ini dijalankan untuk menilai keberkesanan, dan keselamatan regimen pengurusan sakit selepas pembedahan bersalin dalam kalangan pesakit di sebuah hospital di utara Malaysia, Pulau Pinang. Kajian ini juga bertujuan mendokumenkan insidens kesan sampingan opioid dan kesan infeksi di bahagian pembedahan, di samping mengenal pasti faktor risiko mereka. Suatu semakan carta retrospektif secara daripada 400 kes pembedahan semasa bersalin dijalankan di antara Januari 2013 dan Jun 2014. Kajian meneliti demografi pesakit, data obstetrik, pos pesanan sakit koperasi, sebarang infeksi di bahagian pembedahan (surgical site infection, SSI) dan juga kesan sampingan dengan faktor risiko selepas pembedahan. Skor sakit keseluruhan selepas pembedahan dinilai berdasarkan skala analog visual (visual analogue scale, VAS) pada titik masa yang berbeza (2, 4, 8, 12, 24 dan 48 jam selepas pembedahan), iaitu semasa pesakit dalam keadaan berehat dan

bergerak. Keputusan menunjukkan bahawa dalam tempoh 48-jam selepas pembedahan, purata intensiti sakit semasa dalam keadaan rehat dan bergerak adalah masing-masing 0.40 ± 0.013 dan 0.83 ± 0.017. Berdasarkan VAS, analisis sakit semasa rehat menunjukkan bahawa majoriti pesakit 65.9% tidak mengalami sakit (VAS 0), dan 33.6% mengalami sakit yang sedikit (VAS 1-3). Sementara itu, analisis sakit semasa bergerak mendapati bahawa 35.0% tidak mengalami sakit (VAS 0) dan 63.7% mengalami sakit yang sedikit (VAS 1-3). Skor sakit tertinggi bagi kedua-dua keadaan (rehat dan bergerak) adalah pada 12 jam selepas pembedahan. Pelbagai pilihan analgesia yang digunakan dalam pengurusan sakit pasca-CS menunjukkan keberkesanan dan keselamatan dalam kebanyakan kes. Dalam kajian ini, pesakit yang dirawat dengan analgesia kawalan memperoleh skor sakit yang lebih tinggi dibandingkan dengan pesakit yang diberikan epidural atau opioid intratekal. Dapatan kajian menunjukkan bahawa seramai 62 (15.6%) orang pesakit mengalami komplikasi ubat dan terapi, 42 (10.5%) orang pesakit mengalami pruritus, 17 (4.3%) orang pesakit mengalami loya dan muntah, 2 (0.5 %) orang pesakit mengalami retensi urin dan seorang (0.3%) pesakit mengalami hipotensi. Analisis regresi logistik mengenal pasti bahawa, status emosi (anxious) (odds ratio [OR], 6.714; 95% sela keyakinan [CI 95%], 1.42-12.61; P=0.01); indikasi pembedahan (kemajuan / progres lemah) (OR, 5.41; CI 95, 1.33-24.65; P=0.019); kumpulan darah (AB) (OR, 6.73; CI 95, 1.92-10.64; P=0.001); mempunyai kesan yang signifikan terhadap insidens pruritus. Sementara itu, jenis pembedahan (pilihan sendiri / elektif) (OR, 5.75; CI 95,1.13-3.37; P=0.017) didapati mempunyai kesan yang signifikan terhadap insidens loya dan muntah. Sehubungan dengan infeksi, 18.8% pesakit mengalami SSI dan regresi logistik menunjukkan lima pemboleh ubah bebas yang dikaitkan dengan slepas caesarean infeksi tapak pmbedahan. Pemboleh ubah ini adalah

kedudukan bayi yang songsang, intratekal analgesia, sakit yang teruk, anestesia tulang belakang dan tempoh berada di hospital. Sebagai kesimpulan, majoriti pesakit tidak mengalami sakit atau mengalami sakit yang sedikit. menunjukkan bahawa pengurusan sakit selepas pembedahan adalah berkesan dan mencukupi dari segi keperluan keselamatan pesakit.

EVALUATION OF POST-CAESAREAN PAIN MANAGEMENT, PAIN INTENSITY AND RISK FACTOR AMONG PATIENTS IN HOSPITAL PULAU PINANG

ABSTRACT

The caesarean section (CS) rate increased significantly over the past years, accounting for 15 to 25% of births. In the post-CS period, moderate to severe postoperative pain is a commonly reported problem. Good post-CS analgesia improves maternal functional ability and interaction with newborn. There are several analgesic options to optimize pain management, each of them with different efficacy and safety. This study was designed to assess the effectiveness, and safety of postoperative pain management regimen in patients undergoing caesarean section in the obstetric unit of a hospital in the northern part of Malaysia, Pulau Pinang. In addition, to document the incidence of opioid side effect and the incidence of surgical site infection as well as to identify their risk factors. A retrospective chart review of 400 caesarean deliveries was conducted between January 2013 and June 2014. The study reviewed patient's demographics, obstetric data, postoperative pain orders, any surgical site infection (SSI) and any side effect with their risk factors after surgery. The overall pain scores often were assessed by visual analogue scale (VAS) at different time points (2, 4, 8, 12, 24 and 48 hours postoperatively) at rest and with movement. The results demonstrated that within 48 hours post operatively, the average pain intensities at rest and with movement were 0.40 ± 0.013 and 0.83 ± 0.017 (VAS score), respectively. The analysis of pain at rest by VAS showed that

the majority of the patients 65.9% had no pain (VAS 0) and 33.6% of the patients had mild pain at rest (VAS 1-3) while 35.0% had no pain (VAS 0) and 63.7% had mild pain with movement (VAS 1-3). The highest pain score was at 12 hour at rest and movement post-operatively. The various analgesic options used in the management of post-CS pain demonstrated efficacy and safety in the majority of the cases. In this study, patients treated with patient control analgesia had higher pain scores than patients given epidural or intrathecal opioid. Results indicated that 62 (15.6%) of patients complained of different medical and therapy complications, pruritus was present in 42 (10.5%) patients, nausea and vomiting in 17 (4.3%), urinary retention in 2 (0.5 %) and hypotension in one patient (0.3%). Logistic-regression analysis identified that, emotional status (anxious) (odds ratio [OR], 6.714; 95% confidence interval [CI 95%], 1.42-12.61; P=0.01); caesarean indication (poor progress) (OR, 5.41; CI 95, 1.33-24.65; P=0.019); blood group (AB) (OR, 6.73; CI 95, 1.92-10.64; P=0.001); were found to significantly affect the incidence of pruritus, while caesarean type (elective) (OR, 5.75; CI 95,1.13-3.37; P=0.017) was found to significantly affect the incidence of nausea and vomiting. With regards to infection, 18.8% of patients had SSI and logistic regressions showed five variables independently associated with post-caesarean surgical site infection, these variables are breech baby presentation, intrathecal analgesia, severe pain, spinal anaesthesia and duration of hospital stay. In conclusion, as the majority of the patients had none and mild pain, our postoperative pain management was effective and adequate in terms of patients' safety.

CHAPTER 1

INTRODUCTION

1.1 Overview

Postoperative pain is one of the most prevalent forms of pain. Reviewing the literature on management of postoperative pain reveals that more than 50% of patients experience inadequate pain relief after surgical procedure worldwide, despite the introduction of novel agents and analgesic techniques (Lasagna & Beecher, 1954; Warfield & Kahn, 1995). It seems that over the past four decades the under treatment of postoperative pain, in general, has not changed at all.

Postoperative pain can be considered as a major medical, economic and social problem. It causes not only needless suffering in millions of patients worldwide, but also a substantial line of evidence has documented that untreated postoperative pain may account as a significant confounding factor for increased morbidity and mortality, thus resulting in increased length of hospital stay and subsequent higher costs of medical care (Duggleby & Lander, 1994; Wisner, 1990). This evidence has major implications for preventing post-oy tperative complications.

The aims of effective postoperative pain management can be summarized as follows: (a) to provide subjective pain relief while minimizing analgesic-related side effects; (b) to allow early return to normal function and activity by inhibition of trauma-induced nociceptive impulses, which provoke autonomic and somatic reflex responses resulting in cardiovascular, respiratory and neuroendocrine dysfunction; and (c) to reduce side effects related to untreated postoperative pain which may account for increased morbidity and prolonged hospital stay. The treatment of pain is

guided by the history of the pain, its intensity, duration, aggravating and relieving conditions, and structures involved in causing the pain. This needs a wide variety of skills and techniques to treat the pain. These skills and techniques include interventional procedures, medication management, physical therapy or chiropractic therapy, psychological counselling and support, acupuncture and other alternative therapies. All of these skills and services are necessary because pain can involve many aspects of a person's daily life. Pain management has a role in identifying the precise source of the problem and isolating the optimal treatment, in this study we will focus on medication management.

Pain management is considered as an important part of care; pain is now considered the fifth vital sign (Campbell, 1995). The phrase "pain as the 5th vital sign" was initially promoted by the American Pain Society to elevate awareness of pain treatment among healthcare professionals (Affairs, 2000). It is important to emphasize that Pain as the 5th Vital Sign is a screening mechanism for identifying unrelieved pain. Screening for pain can be administered quickly for most patients on a routine basis. As with any other vital sign, a positive pain score should trigger further assessment of the pain, prompt intervention, and follow-up evaluation of the pain and the effectiveness of treatment (Affairs, 2000). The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) implemented pain management standards in 2001 that recognized patients' rights to appropriate assessment and management of pain (William, 2005). The World Health Organization (WHO) reported in 2003 that pain is the leading cause of death and disease burden worldwide (WHO, 2003). Acute pain is still a major factor that annoys both patients

and hospital staff. The intensity of feeling the pain varies from patient to patient, depending on patient's pain threshold, family and hospital staff support.

Pain is a major problem in surgery, including caesarean section; post caesarean section pain is a common cause of acute pain in obstetrics, although pain relief and patient satisfaction are still inadequate in many cases (Control & Prevention, 2005). Today, caesarean section is one of the most frequently performed surgeries in the world (Bloomfield, 2004). Caesarean births are more common than most surgeries, due to many factors. The first factor, of course, is that nearly 50% of the world populations are women, and pregnancy is still a very common condition, However, more important is the fact that a caesarean section may be life saving for the baby, or mother (or both) (Anna'na', 2005).

Postoperative pain after caesarean section (CS) is generally underestimated. Relatively, few studies have been published investigating the different modalities of pain relief after surgical delivery of the neonate (Bick & MacArthur, 2003), however adequate pain relief after low abdominal surgery will improve maternal satisfaction, ameliorate maternal recovery and allow the mother to nourish her new born child. Moreover reduce the risk of thromboembolic disease and infections, which increase during pregnancy (Gilbert, 2007). Following tissue injury, the blood typically becomes hypercoagulable and this can significantly increase the risk of thromboembolism so the early maternal recovery will reduce the risk of thromboembolic disease.

1.2 Definitions of pain

Historically, pain has not been easy to define; it was described purely in terms of its physical nature. During the seventeenth century, pain was viewed as a single of bodily injuries with scant attention being paid to non-physical aspect (Melzack R & Hall, 1996). The first major step forward in the improved definition of pain and in the assessment of pain occurred in May 1972, when John Bonica invited 300 fellow clinicians and researchers together and formed the International Association for the Study of Pain (IASP) (Meldrum, 2003). The IASP Subcommittee on Taxonomy, developed a definition of pain acceptable to both clinicians and researchers: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP, 1979). This definition clearly describes the elements of the pain experience: the unpleasant sensation, the emotional component and the realization that pain can be present without tissue damage.

A more patient-focused definition has been defined by McCaffery (1968) "pain is whatever the person experiencing it says is occurring whenever the experiencing person says it does" has become a cornerstone of the nursing literature (Lellan, 2006). This definition highlights the subjective nature of pain, in addition to its focus on the patient. It is commonly accepted that chronic and acute pain are distinctly different phenomena. Bonica defined acute pain as "a complex constellation of unpleasant sensory, perceptual and emotional experience and certain associated autonomic, psychologic, emotion and behavioral response" (Turk D & Okifuji, 2001). IASP further defined it as "pain of recent onset and probably limited duration which usually has an identifiable temporal and casual relationship to injury and

disease" (IASP, 1992). Chronic pain generally continues past the time of injury and may not have identifiable etiology or may not associate with any overt behavioral sign or physiological change.

1.3 Acute Pain Services:

The development of Acute Pain Services (APS) may be cost effective as well as providing an improved quality of services for patient undergoing caesarean section (Rawal N & Allvin, 1998). JCAHO has issued guidelines for hospital-wide improvement of pain management. The most obvious components of an acute pain team include anesthesiologists, surgeons, nurses, and physiotherapists. Protocols encourage consistent standards of safe and effective care and should be used as a framework to individualize treatment. APS models have been described from USA, UK, Germany, Switzerland and Sweden (Rawal N & Allvin, 1998; William, 2005). Quality hospital care must now include the assessment of pain relief. Effective pain management is fundamental to the quality of care (O'Hara, 1998).

1.4 Pain theories

1.4.1 Specificity theory

The specificity theory proposes that pain is a specific sensation and that the intensity of pain is proportional to the extent of tissue damage. Müller (1842) contributed to the understanding of the sensory process when he recognised that the brain receives information about external objects by way of five sensory systems, seeing, taste, hearing, smell and touch. Von Frey (1894) expanded this and deduced that the skin was comprised of four types of sensory spots that responded to specific

sensations. However, given that this was still focused on the relationship between physical sensation and experience of pain, this theory is not very different to what Descartes proposed centuries earlier (Melzack R & Hall, 1996).

1.4.2 Pattern theories

Goldscheider (1894) for example, was the first to propose that the intensity and frequency of the stimuli (known as pattern of the stimulation), and the brains interpretation of this, are the critical determinants of pain. All pattern theories developed from the premise that stimuli produced a pattern of impulses in neuron's that are transmitted and interpreted as pain (Melzack R & Hall, 1996). Whilst there have been a number of others who contributed to the understanding of pain it wasn't until 1965 when psychologists Melzack and Hall proposed their theory of "The Gate Control Theory of Pain", that the complexity of pain as a problem really begun to be understood (Melzack R & Hall, 1996).

1.4.3 Gate Control Theory

The Gate Control Theory of Pain (Figure 1-1), is an explanation of how the mind plays an essential role in the pain perception. Melzack and Hall (1996) suggested in 1965 that a "gating system" in the central nervous system, opens and closes pain pathways.

The gates can be opened to let pain proceed through the afferent and efferent pathways to and from the brain, or the gates can be closed to block these pain pathways. The gate control mechanism for opening and closing can be influenced by nerve impulses in the efferent pathways.

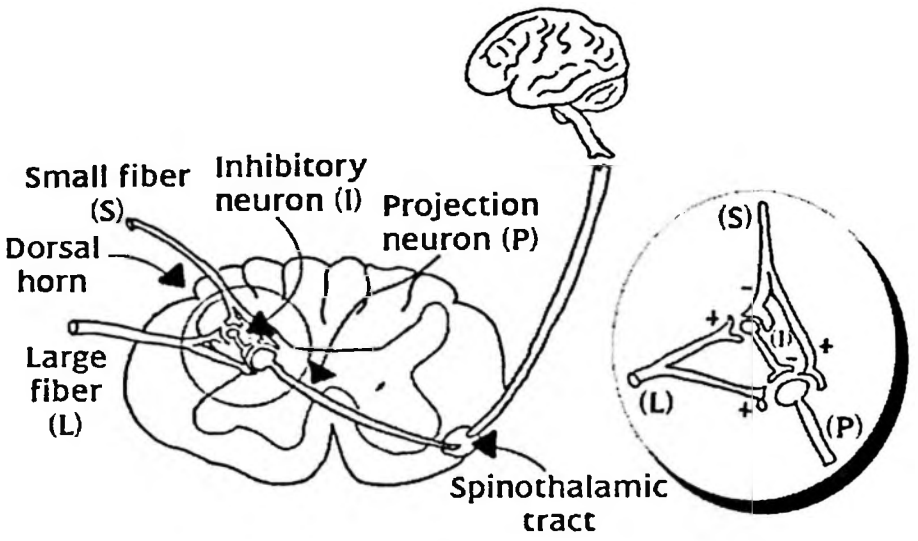

Figure 1.1: "The Gate Control Theory of Pain" adapted from (Melzack R & Hall, 1996)

Efferent nerve impulses are affected by an enormous variety of psychological factors known to influence the brain. Many external factors also impact on the interpretation of pain, such as emotions, or prior experience with pain and anxiety (Montes-Sandoval & Lucy, 1999). This pain theory integrates the physiological, psychological, cognitive, and emotional components that regulate the perception of pain (Melzack R & Hall, 2003).

On the basis of their beliefs about the different types of influences that can alter the perception of pain, Melzack and Hall (1996) postulated that a person could modulate his/her pain using external forces. Their ideas about the interpretative aspects of pain form the basis of the gate control theory. This theory explains why pain is diminished when the brain is experiencing a distracting sensation such as soothing music or the attention of a loved one (stroking or cuddling). In these circumstances, the perception

of pain is decreased because the interpretation of pain is modulated by the distracting pleasant experience. It is this theory that governs current pain assessment and management in health settings. However this is only part of the understanding required to effectively assess and manage pain in patient.

1.5 The pathophysiology of pain

A surgical procedure causes nerve stimulation, tissue injury and damage of small nerve fibers. Consequently, histamine and inflammatory mediators are released. These inflammatory mediators include peptides (e.g., bradykinin), neurotransmitters (e.g., serotonin and ATP), lipids (e.g., prostaglandins), and neurotrophins (e.g., nerve growth factor) (Julius & Basbaum, 2001; Miller *et al.*, 2010). This "inflammatory soup" interacts with receptors or ion channels on sensory nerve endings (peripheral nociceptors) (Figure 1-2) (Julius & Basbaum, 2001; Sinatra & de Leon-Cassasola, 2009). Nociceptors may release peptides and neurotransmitters [e.g., substance P, calcitonin-generelated peptide (CGRP) and ATP] locally when they are activated by noxious stimuli. This process is called neurogenic inflammation and induces vasodilatation and plasma extravasation (Figure 1-2) (Julius & Basbaum, 2001).

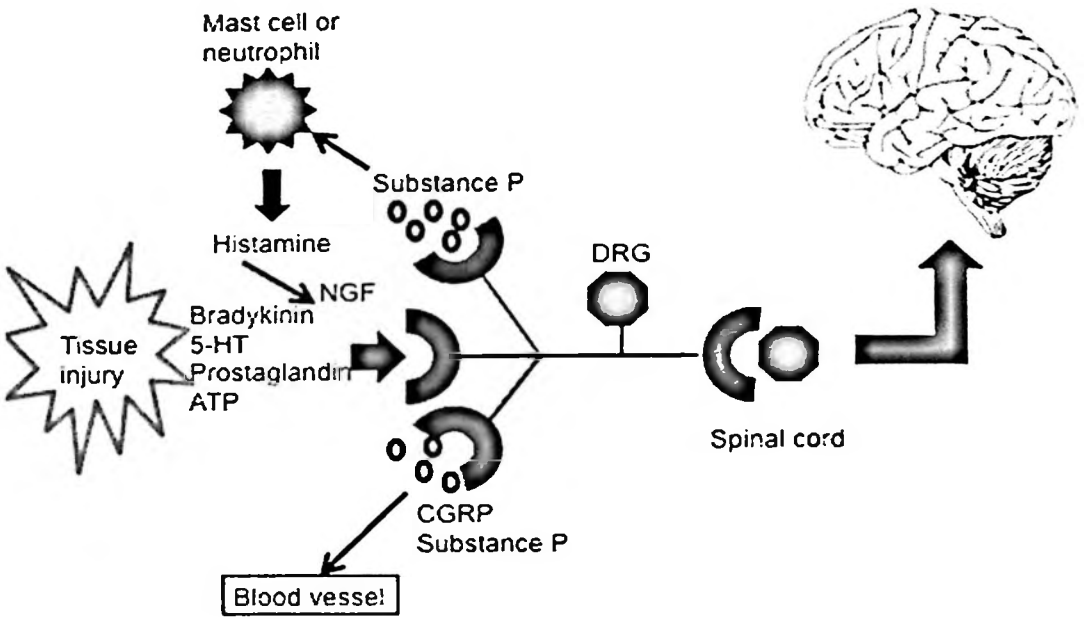

Figure 1.2: The 'inflammatory soup': adapted from (Julius & Basbaum, 2001)

Peptides (bradykinin), lipids (prostaglandins), neurotransmitters [serotonin (5-HT) and ATP] and neurotrophins (NGF) are activated by tissue injury and lower the threshold (i.e., sensitization) or excite the terminals of the nociceptor by interacting with cell-surface receptors. Nociceptor activation transmits afferent messages to the dorsal horn of the spinal cord and further to the brain. The activation of peripheral nociceptors by noxious stimuli is termed transduction. Further delivery of noxious stimuli as an action potential from peripheral somatic and visceral sites to the dorsal horn of the spinal cord via Aδ and C nerve fibers is called conduction, whereas the synaptic transfer of noxious impulses to secondary-order cells in the dorsal horn is termed transmission (Figure 1-3) (Miller *et al.*, 2010; Sinatra & de Leon-Cassasola, 2009). Transmission of nociceptive information undergoes complex modulation in the spinal cord.

Although some impulses pass to the ventral and ventrolateral horns and initiate segmental (spinal) reflex responses, it is assumed that most impulses are propagated to higher neuronal centers. This transmission is mediated via the spinothalamic and spino-reticular tracts and induces supra-segmental and cortical responses. This will finally lead to the perception of pain (Miller *et al.*, 2010).

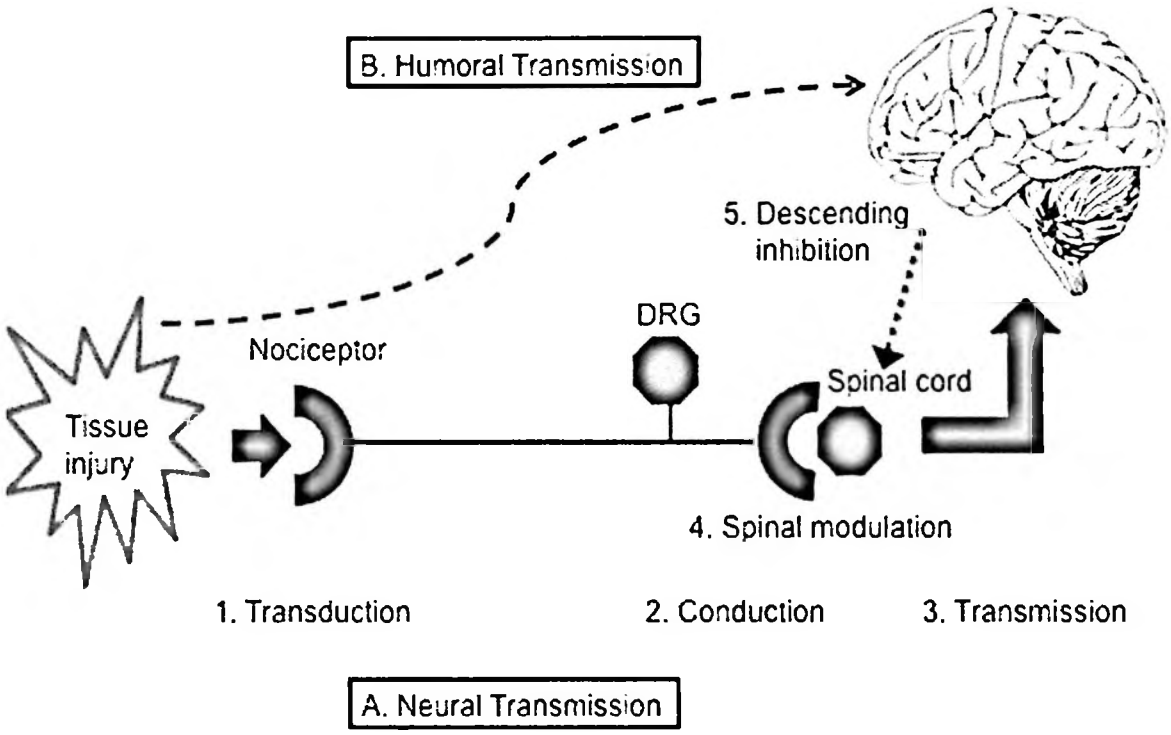

Figure1.3: Overview over pain perception adapted from (Miller *et al.*, 2010; Sinatra & de Leon-Cassasola, 2009)

A. Neural Transmission:

1. Transduction: Tissue trauma causes the releases of noxious mediators, which activate the terminals of the nociceptor.

2. Conduction: Noxious impulses are delivered to the dorsal horn of the spinal cord

3. Transmission: Synaptic transfer to the central nervous system.

4. Modulation: Spinal interneurons facilitate this noxious transmission.

5. Descending inhibition: CNS structures suppress pain transmission.

B. Humoral transmission: Tissue injury results in humoral transmission of noxious mediators to the CNS. DRG = Dorsal Root Ganglion

Repeated or prolonged release of inflammatory mediators in the periphery may sensitize functional nociceptors. This sensitization is characterized by decreased activation threshold, increased discharge rate, and increased basal discharge. Furthermore, continuous nociceptive activity may activate dormant nociceptors and subsequently shift the dorsal horn to sensitized modes (Carr & Goudas, 1999; Miller *et al.*, 2010; Woolf & Mannion, 1999).

The phenomenon of neurohumoral alterations at the site of injury is called peripheral sensitization and may be responsible for primary hyperalgesia (Sinatra & de Leon-Cassasola, 2009; Woolf, 1995). Hyperalgesia is defined as "an altered state of sensibility in which the intensity of discomfort associated with repetitive noxious stimulation is markedly increased" (Sinatra & de Leon-Cassasola, 2009). Intensive noxious stimulus from the periphery may also result in exaggerated dorsal horn responses to Aβ-fibre input (Woolf & Mannion, 1999). This process is called central sensitization and will cause secondary hyperalgesia, which refers to an alteration in noxious sensitivity in non-traumatized regions (Sinatra & de Leon-Cassasola, 2009; Woolf, 1995).

1.6 Caesarean section

1.6.1 Definition of Caesarean Section CS

More incision are made through a mother's abdomen (laparotomy) and uterus (hysterectomy) to deliver one or more babies, or, rarely, to remove a dead fetus. A late-term abortion using caesarean section is termed a hysterectomy abortion and is very rarely performed (Shearer, 1993).

1.6.2 History of caesarean section and development of modern operative obstetrics

Probably the very first documented evidence of caesarean birth is a legal text dating to the era of Hammurabi (1795-1750 BC), describing the birth of a male child "pulled out of the womb" of a deceased woman (Lurie, 2005). The name sectio caesarea was first used by the French obstetrician Guillimeau in 1598. At that time, the operation was used to deliver live babies from dead mothers (O'sullivan, 1990). There are three different explanations about the origin of the name of the operation. In 715 BC, the King of Rome, Numa Pompilius, codified the Roman laws. According to the law, it was forbidden to bury a dead pregnant woman before the foetus was excised. If the child was alive, it was called a "caeson". This law, Lex Caesaris or Lex Caesarea, is assumed to be the origin for the name of the procedure "cesarean section" (Lurie, 2005; O'sullivan, 1990; Todman, 2007).

It has also been stated, that Julius Caesar has been delivered by this method, and gave the name for the operation. This is considered unlikely, because his mother is known to have been alive during Julius Caesar's adulthood. During his reign about 100 BC no woman is known to have survived the operation. A third explanation is that the name is simply derived from the Latin verb caedare, to cut. The word "section" is also derived from the latin verb secare, to cut (O'sullivan, 1990).

In the early 1900s, DeLee of USA, the foremost academic leader in obstetrics of his time, implemented an attitude that most pregnancies are potentially abnormal and must be managed by experts in order to achieve good results. Obstetrics became a specialty practiced by surgeons (Cyr, 2006). In the latter half of the1900s, specialist units were increasing and pregnant women chose often to have birth in hospitals. The units were staffed by a consultant surgeon or an obstetrician, and soon also by consultant anaesthesiologist. Operative obstetrics became a part of the functions of a modern hospital. The rate of CS rose concomitantly with an active policy of interventions. The need for interventions rose in pace with increased inductions, an established definition of prolonged labour and electronic fetal monitoring. In many countries "defensive obstetrics" became a common phenomenon, increasing rate of CS because of fear of litigation related to claimed negligence of fetal safety (O'sullivan, 1990).

1.6.3 Indications for caesarean section

Before the 1800s, CS was performed only after the death of the mother to give the baby a chance to survive (Lurie, 2005; O'sullivan, 1990) . In the 1800s, CS was sometimes performed for maternal reasons for obstructed labor, usually after the labor had been going on for several days. By the early 1900s, CS was performed for placenta Previa, eclampsia, difficult labor and sometimes even at the mother ´ s request (Cyr, 2006). As mortality has declined, the indications for CS have shifted more to the benefit of the neonate.

In the late 20th century and during the recent years, the main indications for a CS have been protracted labour, (suspected) fetal distress, mal-presentation of the

foetus, placental abnormalities and maternal reasons (Kolås *et al.*, 2003; Stjernholm *et al.*, 2010). Since focus has been increasingly put on foetal wellbeing, breech presentation has become a common indication for a CS, particularly after publication of the Term Breech Trial by Hannah et al. (Hannah *et al.*, 2000). Although the transverse lower uterine segment incision has led to a substantially lower risk of uterine rupture in subsequent deliveries compared to earlier techniques, a uterus scarred by previous CS has become one of the most common indications for CS in many countries (MacDorman *et al.*, 2008) (Fitzpatrick *et al.*, 2012).

Towards the end of the 20th century, a new indication emerged and increased the rate of CS in many countries: CS without medical indications or CS for maternal request. This has led to controversies among obstetricians, with some accepting this policy and some not. Although there is evidence of higher maternal morbidity and even mortality related to CS compared to vaginal birth (VD), many patients and even obstetricians consider it safe enough to be performed even without any specific indication (Gunnervik *et al.*, 2008; Habiba *et al.*, 2006).

For the low-risk group of women with no indication for a CS, the rate of CS has been rising, and is estimated to be about 7% of all CS in the US in the early 2000s (Bailit *et al.*, 2004; MacDorman *et al.*, 2008; Menacker *et al.*, 2006). Still, a US survey showed that a much smaller proportion of all women were interested in a non-indicated CS in the early pregnancy, suggesting that this trend is partly driven by the obstetricians themselves (Menacker *et al.*, 2006).

Caesarean section because of fear of delivery has become a common indication for CS, especially in the Nordic countries. In Finland, where there is more than ten years of experience of active management of fear of delivery to support parents and

to avoid unnecessary CS, in average 1% of all deliveries are CS performed for this indication (Rouhe *et al.*, 2007). In Sweden the indication "fear of childbirth or maternal request" has increased from 0.6% to 3.9% of all deliveries from 1992 to 2005 (Stjernholm *et al.*, 2010). To which extent "fear of delivery" overlaps the indication "maternal request" used in many countries is not known, but a Swedish study on the subject showed, that 43% of women requesting a CS showed a clinically significant fear of delivery (Wiklund *et al.*, 2008).

1.6.4 Prevalence of caesarean section

In 1985, The World Health Organization (WHO) issued recommendations about appropriate technology for birth, and stated that there is no justification to have a caesarean section rate of higher than 10%. This was subsequently increased to 15%, taking into consideration the higher incidence of cephalopelvic disproportion (CPD) and human immunodeficiency virus (HIV) found in many developing countries (WHO, 1985).

Over the past twenty years, the caesarean section rate has continued to increase dramatically, in both developed and developing countries. In the United Kingdom, the caesarean section rate increased from 4,5% in 1970 to over 20% in 2005 (Thomas & Paranjothy, 2001). In 2007, the average rate of caesarean deliveries in Europe was recorded at 19%, with Italy showing the most marked increase from 11,2 % in 1980 to 36% in 2007 (Parazzini *et al.*, 1992). The caesarean section rate in the United States increased almost fivefold between 1965 and 1990, rising from 4.5% in 1965 to 22.7% in 1990 with over one fourth of the four million live births by caesarean section (Taffel, 1994), The rate has increased to 33% of all births in 2012 (Caughey *et al.*, 2014). In Australia the caesarean delivery rate is 21.6%, and similarly, in

Canada 22.5%. Whilst the average caesarean section rate for Asia is reported at 15.9%, rates in excess of 40% have been estimated for China (Betrán *et al.*, 2007).

There was a report on the caesarean section rates in government hospitals in Malaysia for the period 2000 to 2001. The caesarean section rate rose from 10.5% in 2000 to 11.1% in 2001(Ravindran, 2003). The rates have increased up to 15.7% in 2006. There are inter-state variations in the rate ranging from 25.4% in Melaka to 10.9% in Sabah. The West Coast states generally had a higher caesarean section rate than the East Coast states as well as East Malaysia. In Penang the rate rose from 12.5 % in 2000 to 17.4 % in 2006 (Ravindran, 2008).

The dramatic rise in the caesarean birth rate can partly be explained with increased use of technical, medical equipment. During the labour, it is now easier to discover risks concerning the mother and the baby earlier. The increase can also be explained with increasing age among mothers, maternal request, that more woman have had previous caesarean section, and because it has become more common with multiple babies.

1.6.5 Complication of caesarean section

2.1.5(a) Hemorrhage

In most studies, hemorrhage is the most common cause of morbidity related to delivery. The reported incidence of hemorrhage and severe hemorrhage related to delivery varies markedly by study. This is partly explained by different definitions. The following definitions of hemorrhage have been used in the different studies: defined ICD-codes, >500ml, >1000ml, >1500ml, any transfusion of blood,

transfusion of ≥4 units red cells, fall in the haemoglobin concentration ≥40 g/l, embolization or hysterectomy for hemorrhage, re-operation for hemorrhage (Häger *et al.*, 2004; Holm *et al.*, 2012; O'Brien *et al.*, 2010; Waterstone *et al.*, 2001; Zwart *et al.*, 2008). The amount of hemorrhage is often estimated visually, which is known to be inaccurate, and the amount of PPH is often over- or underestimated, more often underestimated, which can cause a delay in the proper care of the woman (Kabel & Weeber, 2012; Prasertcharoensuk *et al.*, 2000). Some of the variation may depend on variation in the quality of obstetric care. In a register based cohort study in California, USA, comprising 507 410 births in 1997, postpartum hemorrhage complicated 2.4% of births. The incidence varied up to 3-fold by hospitals even after adjusting for risk factors. The authors suspect that this is partly due to improper conduct of operative deliveries (Lu *et al.*, 2005).

When hemorrhage was defined as ≥1000ml and/or a need for transfusion, Hager et al found that the incidence was 8.6% related to CS in a prospective study while Källen reported 13% in a register based study (Häger *et al.*, 2004; Källén *et al.*, 2005). Some studies report a lower incidence of haemorrhage in elective CS than in VD, but usually higher incidence of transfusions (Koroukian, 2004). Still, most studies report a higher incidence of any haemorrhage in CS, even in elective CS, although haemorrhage is even more often related to emergency CS than elective CS. When the most severe forms of haemorrhage (haemorrhage leading to hysterectomy or other interventions) are studied, the incidence is 6-14-fold in all studies even for primary CS compared to VD, and still higher after a previous CS (Knight *et al.*, 2008; Simoes *et al.*, 2005).

Haemorrhage is often defined as severe in following cases: >1500ml, (Stivanello *et al.*, 2010) transfusion of ≥4 units red cells, fall in the haemoglobin concentration ≥ 40 g/l., embolisation or hysterectomy for haemorrhage and in case of re-operation for haemorrhage (Häger *et al.*, 2004; Waterstone *et al.*, 2001; Zwart *et al.*, 2008). In a British study the incidence of severe obstetric haemorrhage (>1500ml, ≥four units of blood, fall in HB ≥40 g/l) was 0.7% in all deliveries, more frequent in CS than in VD and most frequent in emergency CS (Waterstone *et al.*, 2001).

2.1.5(b) Intra-operative complications

The incidence of intra-operative complications was 14.8% in a study of 2647 CS in a university hospital in Netherlands 1983-1992. The complications included blood loss ≥1000 ml, accidental incision of the foetal skin (1.3%), lacerations of the uterine corpus (10.1%), bladder lesions (0.8%), laceration of uterine arteries or laceration to the bowels (0.5%). Complications were more common in emergency operations than elective operations and more common in women with a prior CS than among women without a prior CS (Van Ham *et al.*, 1997).

2.1.5(c) Complications of anaesthesia

In a US study on anaesthesia-related maternal mortality in 1991-2002 there were 1.2 anaesthesia-related maternal deaths per 1,000 000 live births, comprising 1.6% of all pregnancy related deaths. The number has decreased by 59% since 1979-1990. The leading cause of death was intubation failure or induction problems, followed by respiratory failure, high spinal or epidural block and drug reactions. A total of 86% of these deaths were related to CS (Hawkins *et al.*, 2011).

In a district hospital in the UK accidental dural punctures and post dural puncture headache in obstetric anaesthesia was followed over a 23-year period (1993-2006). The occurrence of accidental dural punctures after epidurals in all obstetric procedures was 0.9%; 88% of these patients experienced post dural puncture headache which required an epidural blood patch (Sprigge & Harper, 2008).

In 1990-1991 data was collected in 79 obstetric units in the UK, and among 123 000 women receiving either epidural or spinal blockade in obstetric care, 1/1000 had a severe complication, post dural puncture headache not included. The complications were neuropathies of single nerves in 46 women, unexpectedly high blockades in 26 women, backache in 21 women, urinary retention in 8 women, two women with cardiac arrest and one women with maternal death (Scott & Tunstall, 1995).

2.1.5(d) Infections

In the recent decades, the use of prophylactic antibiotics during deliveries has increased. The use of prophylactic antibiotics related to CS is widespread, especially during emergency procedures. The infection rate related to CS has decreased with the prophylactic use of antibiotics (Hofmeyr *et al.*, 2008).

The different rates of infections reported in different studies are partly explained by the variable observation periods. The duration of the hospital stay has become shorter during the recent years. In a Danish study on postpartum infections with a follow-up time of 30 days after delivery, the investigators noticed that 77% of postpartum infections appeared after hospital discharge. The risk of postpartum infection was five times higher after CS than after VD (Leth *et al.*, 2009). Also in a Norwegian study on surgical site infections, 20 % of all wound infections were diagnosed during

the hospital stay and 80% later, during a 30 days follow-up time (Kristian Opøien *et al.*, 2007).

In the prospective Norwegian study by Häger et al, 7.0% of the women had an infection after CS during the hospital stay (Häger *et al.*, 2004). In a Canadian study by Allen et al. the incidence of puerperal febrile morbidity and wound infection combined was 0.6% in spontaneous VD, 2.6% in elective CS and 5.5% in CS in labour (Allen *et al.*, 2003). In the Danish study by Krebs et al, puerperal febrile morbidity and the incidence of wound infection combined was 1.2% in VD, 2.4% in elective CS and 4.1% in emergency CS (Krebs & Langhoff-Roos, 2003). In the US study by Koroukian, the incidence of major puerperal infection was 0.9% in VD, 2.9% in elective CS and 4.3% in emergency CS (Koroukian, 2004).

In a Cochrane review covering 86 randomized trials that compared antibiotic prophylaxis with no prophylaxis for elective and non-elective CS, prophylactic antibiotics did reduce the incidence of febrile morbidity significantly (RR 0.45) both in elective and emergency CS (Smaill & Gyte, 2010)..

2.1.5(d)(i) Surgical Site Infection (SSI)

Surgical site infection (SSI) is defined as an infection occurring within 30 days after a surgical operation (or within 1 year if an implant is left in place after procedure) and affecting either incision or deep tissues at the operation site (Mangram AJ *et al.*, 1999). These infections may be superficial (those involving only the skin or subcutaneous tissue) or deep incisional infections (those involving deep soft tissues of an incision) or infections involving organs or body spaces (Horan *et al.*, 1992). Postoperative SSI is among the most common problems for patients who

undergo operative procedures and the third most frequently reported nosocomial infection in the hospital population (Mangram AJ *et al.*, 1999). It is associated with increased morbidity, mortality, prolonged hospital stay and increased economic costs for patient care (Weigelt *et al.*, 2010).

There has been advance in SSI control practices, which include improved operating room ventilation, sterilization methods, use of barriers, surgical technique and availability of antimicrobial prophylaxis. Despite, these SSIs remain common causes of morbidity and mortality due to emergence of antimicrobial resistant pathogenic bacteria (Mangram AJ *et al.*, 1999). This is partly contributed by inappropriate use of surgical antimicrobial prophylaxis (Al-Momany *et al.*, 2009).

SSIs can be reduced by appropriate use of surgical antimicrobial prophylaxis. In hospital practice, 30-50% of antibiotics are prescribed for surgical prophylaxis and 30-90% of this prophylaxis is inappropriate (Munckhof, 2005). This inappropriate use increases selection pressure favoring emergence of pathogenic drug resistant bacteria (Al-Momany *et al.*, 2009) which makes the choice of empirical antimicrobial agents more difficult and hence increasing the risk of post-operative wound infections.

In a Norwegian study on surgical site infections, the total rate of wound infections related to CS was 8.9% during a 30 days follow-up time, but at hospital discharge only 1.8% (Kristian Opøien *et al.*, 2007). The risk of wound infections increased significantly in obese women also when the operating time exceeded 38 minutes. There was no difference in wound infection rate between elective CS and emergency CS (Kristian Opøien *et al.*, 2007).

2.1.5(e) Infant risks

Neonatal mortality rates for CS births were significantly higher than for vaginal births (2.85 vs. 1.83 per 1,000 live births according to MacDorman et al 2006 (MacDorman *et al.*, 2006). MacDorman and his colleagues studied a cohort of 5.7 million births to low risk women in the United States. Kolas and colleagues (2006) reported that infants born by planned CS had approximately double (9.8% vs. 5.2%) the risk of admission to the neonatal intensive care unit than infants born by vaginal delivery. Kolas et al. used a sample size of 18,653 in this study. Infants had twice the risk of serious breathing difficulties in the planned caesarean group (Kolås *et al.*, 2006).

Infants born via CS are at increased risk for many complications, including a delay in maternal bonding caused by a prolonged time between birth and the mother holding the infant (Rowe - Murray & Fisher, 2001). In addition, Rowe-Murray and Fisher (2001) reported a decrease in mother-baby skin-to-skin contact after CS compared to a vaginal delivery group. Breastfeeding is an important source of nutrition for the infant, as well as immunity and positively affects maternal-infant bonding. Infants born by maternal request CS had a significant delay in initiation of breastfeeding (Cakmak & Kuguoglu, 2007; Rowe - Murray & Fisher, 2002). Dewey et al 2003 reported that infants born via CS had suboptimal breastfeeding behaviors, excessive weight loss, and the mothers had delayed onset of lactation (Dewey *et al.*, 2003).

1.7 Post-caesarean pain

Post-caesarean pain is likely to have at least two components (Lavand'homme,

2006), with pain arising from both the abdominal and uterine incisions, with a third potential source being pain associated with uterine involution post-delivery (Pavy *et al.*, 1995). Somatic pain arising from nociceptors within the abdominal wound has both cutaneous and deep components. It is transmitted within the anterior divisions of the spinal segmental nerves, usually T10-L1, which run laterally in the abdominal wall between the layers of the transversus abdominis and internal oblique muscles (McDonnell *et al.*, 2007). Visceral uterine nociceptive stimuli return via afferent nerve fibres that ascend through the inferior hypogastric plexus and enter the spinal cord via the T10-L1 spinal nerves (Moore, 1992).

Traditionally it has been difficult to predict the severity of post-caesarean pain and analgesic needs because of large interpatient variability in the intensity of pain experienced, as well as difficulties in predicting the response to an individual analgesic regimen. Factors that have been associated with significant post-operative pain have included the duration of surgery, probably as a consequence of more extensive dissection, and a lower dermatomal level of sensory anaesthesia at the time of incision, which may contribute to greater nociceptive input to the spinal cord and enhanced central sensitization (Eisenach *et al.*, 2005). A series of pre-operative physical (thermal pain threshold) and psychological tests have been shown to predict the upper 20th percentile of post-caesarean pain scores with a sensitivity of between 0.71-0.80 and a specificity of 0.76 to 0.80, and to show improved prediction over single test models (Granot *et al.*, 2003; Pan *et al.*, 2006).

An ideal post-caesarean analgesic regimen would be one that was cost effective, simple to implement and with minimal impact on staff workload. It would provide consistent and high quality pain relief whilst catering for wide interpatient

variability yet has a low incidence of side effects and complications. It would not interfere with the maternal care of the new-born or with the establishment of breast feeding and there would be minimal drug transfer into breast milk and no adverse effects on the new-born. In this regard, a multimodal approach based on opioids has been commonly recommended (Lavand'homme, 2006; Pan, 2006).

1.8 Type of medication

An analgesic or painkiller is any member of the group of drugs used to achieve analgesia, relief from pain. Analgesic drugs act in various ways on the peripheral and central nervous systems. They are distinct from anesthetics, which temporarily affect, and in some instances completely eliminate, sensation. Analgesics include paracetamol, the nonsteroidal anti-inflammatory drugs (NSAIDs) such as the salicylates, and opioid drugs such as morphine and oxycodone. In choosing analgesics, the severity and response to other medication determines the choice of agent; the World Health Organization (WHO) pain ladder (WHO, 1990).

Paracetamol: also known as acetaminophen, it is typically used for mild to moderate pain. In combination with opioid pain medication, paracetamol is used for more severe pain such as cancer pain and after surgery (SIGN, 2008). It is typically used either by mouth or rectally but is also available intravenously (Tobias *et al.*, 2014). Effects last between two and four hours (Tobias *et al.*, 2014). Paracetamol is classified as a mild analgesic and is generally safe at recommended doses (Tobias *et al.*, 2014).

Nonsteroidal anti-inflammatory drugs (usually abbreviated to NSAIDs), are