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Hysterectomy: Advances in Perioperative Care

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1. Introduction

1.1 Perioperative medicine

Perioperative medicine is an ever growing field of interest that encompasses the care of the patient preparing for, undergoing and recuperating from surgery. Medical professionals, interest groups and societies each year convene at congresses dedicated to the field of evidence-based perioperative medicine (e.g., www.ebpom.org). Since many interventions during the hospital stay have ramifications extending into the first six months after discharge, many choose to define "perioperative" broadly to include this extended period as well. Our topics of interest are equally broadly defined and include psychological, physiological, anaesthesiological and surgical issues. We have chosen this overview to increase our understanding of the interplay of factors that in all make up the experience of the hysterectomy patients, hopefully to explain and justify the value of treatment regimens.

1.2 Purpose and methods

Much has happened within the past 10 years. In spite of an ever-growing and unwieldy amount of scientific information appearing every month, unmet needs may still be readily identified in many fields of endeavor. To highlight the current evidence, we have performed a Medline search on "hysterectomy" limited to randomized studies published in the past decade. This should expand the evidence-based website www.postoppain.org, which provides an analysis of all randomized studies on abdominal hysterectomy since 1966 (and until 2004). Our aim is to provide the anaesthesia-unqualified reader with an extensive and easily accessible presentation of the psychology, physiology, pharmacology and operative logistics that we find relevant to the subject of hysterectomy; characteristics of the patients, the importance of anaesthetic and surgical techniques, the prevention and treatment of postoperative complaints, and why established treatments may not work. While not striving to be completely exhaustive, our review nevertheless includes a thorough reference list that may inspire the reader to further in-depth study.

2. Psychology

2.1 Preoperative psychology and coping skills

Understandably, undergoing surgery is often the cause of great concern for patients. We know that as many as 60% of patients are anxious (Hashimato, 1993), with females, depressed and

patients in pain being particularly prone (Caumo, 2002; Karanci, 2003). This anxiety is caused by uncertainty/lack of information about what is going to happen and an existential component (Caumo, 2002; Sjölin, 2003). While uncertainties about oncoming events may be reduced by relevant information and proper expectations, existential anxieties are often resistant to intervention (Kain, 2001). Studies have shown that most patients are scared of thoughts of the unknown, severe pain, nausea and vomiting, or imminent death (Kindler, 2000). Previous experiences and personality usually dictate the style and ability of coping and dealing with serious life events such as surgery. Studies using the Spielberger State and Trait Anxiety Index (Johnson, 1968) or the Amsterdam Preoperative Anxiety and Information Scale (Moerman, 1996) have documented that particular personality structures and coping skills of the patient are in part responsible for the intensity and duration of postoperative pain, with subsequent self-imposed limitations to mobilization and restoration of normal activities (Riddle, 2010). Such psychological traits may in fact be so strong that they overshadow effective pain treatment (Maranets, 1999; Caumo, 2002; Kalkman, 2003). Neurologically, the interaction between the amygdala (fear-avoidance centre), the frontal cortex (centre of experience and value-setting), and the nucleus accumbens (reward centre) are pivotal, all of which are influenced by personality, obesity, alcoholism, depressive disorders and more (Di Chiara, 2002). The personality structure that is most reliably used is the five factor model (Big Five Inventory) which uses five independent personality measures (openness to change, conscientiousness, extroversion, agreeableness, and neuroticism) (Digman, 1990). The variability of these measures is dynamic, and at least three measures rapidly change following surgery: patients become less open to changes, more introvert, and more negative in thought. These changes lead to distorted and inefficient coping skills, depressive or defeatist mood swings, and catastrophizing (imagining unlikely and potentially catastrophic events from simple and harmless signs and symptoms). These emotions are strong and overwhelming and must be addressed in order to secure a return to postoperative well-being.

2.2 The impact on postoperative well-being

Preoperative pain or depression may be seen in as many as 50% (Davies, 2002). In a study on chronic pain following hysterectomy, most patients having pain at four months after surgery had pain that resembled the preoperative pain; preoperative "pain problems elsewhere" and strong acute postoperative pain were associated with the development of chronic pain, again emphasizing the psychological dimension (Brandsborg, 2009). Women with preoperative depression and pain had 3 to 5 times the odds of continued impaired quality of life for both physical function, mental health, social function and dyspareunia, compared to those who did not have depression or pain (Hartmann, 2004). The extent (subtotal vs total hysterectomy) or method (laparoscopic vs abdominal) of surgery does not seem to influence these long-term effects (Thakar, 2004; Flory, 2006). Most studies support a general increase in psychosocial well-being at 6 months following surgery (Davies, 2002; Persson, 2010), and it is worth noting that this long-term well-being does not seem to be associated with perioperative complications or hormone disturbances (Persson, 2010).

2.3 Long-term psychological effects following hysterectomy

Women undergoing hysterectomy are in a particularly difficult position, since surgery may alter both their perception of body image and sexuality, and impose hormonal

changes after oophorectomy with surgical menopause. As a case in point, quality-of-life estimates are clearly rated as worse by a surgical menopause than by a natural menopause (Bhattacharya, 2010). Surgical menopause also adversely affects perceptions of body image and sleep quality at six months compared to ovarian conservation surgery (Teplin, 2007). Women who undergo prophylactic oophorectomy in addition to hysterectomy are found to have higher anxiety-related scores, lower sexuality scores and poorer emotional partner relationships (Aziz, 2005). In terms of sexual function, extent of surgery (subtotal vs total hysterectomy) does not seem to affect overall sexual activity, but total hysterectomy does reduce the perception of body image at one year (Gorlero, 2008). Recently, however, some have found that women who had subtotal hysterectomy report significantly greater positive change in the frequency of orgasm and sexual pleasure than women who have had total hysterectomy (Ellström, 2010). Method of surgery (laparoscopic vs vaginal vs abdominal) yields conflicting results on the influence on sexual activity (Ellström, 2003; Roovers, 2003). Women having abdominal hysterectomy may be dissatisfied with their body image because of the abdominal scar (Gütl, 2002). Quality of life following hysterectomy for malignant reasons seems to be affected even stronger: sexual function worsens considerably, regardless of surgical technique (Serati, 2009). Anxiety and depression following surgery for cervical cancer is commonly associated with financial difficulty, poor body image, sexual inactivity, and low existential well-being. Low support and insomnia are related to anxiety, with older age and decrement role function related to depression (Kim, 2010). These substantial effects seem to cling to an inherent personality profile rather than disease-related clinical factors.

2.4 Prevention and treatment of anxiety and its effects

Trait and existential anxiety seem to be resistant to preventive informational or cognitive interventions. Procedure-specific concerns, however, lend themselves to several psychological og medical approaches (Caumo, 2002). A preoperative 24-minute videotape of a nurse showing breathing and movement skills with four postoperative mobility activities (The Foster Pain Intervention) reduces pain, increases mobility, preoperative self-efficacy and speeds up home readiness more than a control group receiving standard information (Heye, 2002). Cognitive interventions using distraction and reappraisal combined with information are associated with lower postoperative anxiety, less pain and higher levels of satisfaction (Cheung, 2003). Therapeutic touch may be equally effective (Vitale, 2006). Intraoperative music is associated with increased levels of sedation and satisfaction (Zhang, 2005). Patient-carer interactions using negative words on the surgical wards has significant influence on pain in the early postoperative period by increasing pain, opioid consumption and stress hormone levels, whereas positive words or no words at all has little influence (Wang, 2008). These studies again underline the importance of optimal information-handling, pragmatic instructions, simple psychological interventions and decent patient-carer interactions as the basic premise for the prevention of postoperative complaints following hysterectomy. It makes perfect sense to identify beforehand the psychological traits that predispose to inappropriate coping abilities, exaggerated pain processing and distorted body image perceptions, since they seem to share similar psychological profiles (Persson, 2008).

3. Pharmacology

3.1 Opioid-free analgesia

Opioid-free analgesia has long been considered the holy grail of pain treatment. Opioids reduce nociceptive signal processing in the spinal cord and central nervous system by acting on, among others, the μ receptor. The analgesic potential for blockade of this receptor is limitless, and the mode of administration of an opioid is largely independent of its efficacy. No other type of drug has a similar potential, and for this reason, opioids are of immense value. Opioids are widely distributed and are subsequently found in most compartments of the body by any route of administration. In terms of analgesic effect, no strong opioid is superior to any other; their only differences rest in mode of administration, dosage and duration of action (Macintyre, 2010). Surgical stress and analgesic efficacy during and after abdominal hysterectomy proceeds regardless of the opioid used (Rodriguez, 2007); one report argues that morphine in combination with the weak opioid tramadol may confer better postoperative pain scores than morphine alone (Kocabas, 2005), but the result should be replicated before firm conclusions can be made. Spinal morphine seems to attenuate several measures of the surgical stress response, in particular serum values of catecholamines and glucose (Karaman, 2006). However, preoperative intravenous morphine fails to attenuate the stress response measured by serum cortisol, glucose and leukocytes (Kilickan, 2001); the socalled "preemptive effect" has been largely abandoned in clinical life because many studies fail to document better pain relief when opioids are administered preoperatively than postoperatively, even though studies appear from time to time arguing the case of preemptive analgesia from the viewpoint of minor effects on immune function, parameters which may be clinically redundant (Akural, 2002; Akural, 2004).

3.2 Opioid side effects and preventive strategies

In terms of side effects, however, opioids do have differences, primarily due to pharmaco-kinetics (administration, distribution, metabolism, excretion), where the most basic opioid, morphine, may accumulate metabolites that are neurotoxic under certain conditions such as renal insufficiency, advanced age or immense doses (Murphy, 2005). The quest for opioid-free analgesia, however, stems from the autonomic side effects of the drugs: impaired cognitive function, dizziness, sedation bordering on coma; respiratory depression and apnoe; nausea, vomiting and increased gastrointestinal sphincter contraction causing obstipation; urinary bladder paralysis, pruritus and excessive sweating. Many of these side effects occur at random and with different intensities, but they all counteract the primary content of recuperation: eating, drinking, passing urine, defecating and ambulating. All opioids act similarly in this respect, and although side effects usually occur at higher doses than analgesic effects, they still remain a major clinical problem which render many patients helpless, unable to get out of bed, with the subsequent risk of more severe complications such as hypoxia, pneumonia, deep venous thrombosis, pulmonary embolism, ileus and decubitus. The apparent discord between the obvious need for opioids and the abhorred side effects have led clinicians to try various methods of alleviating opioid-related side effects: 1) the combination of intravenous morphine with a μ-receptor antagonist such as naloxone by patient-controlled analgesia (PCA) has been largely disappointing (Sartain, 2003; Zhao, 2005); 2) a similar combination using a μ-receptor antagonist, alvimopan, with limited oral bioavailibility (thus only acting in the GI tract) has fared better and has been

shown to improve tolerance to solid foods, time to first bowel movement and passage of stool, although the magnitude of improvements were moderate (Herzog, 2006; Tan, 2007); 3) the use of simple osmotic laxatives have been shown to reduce time to first defecation from 69 to 45 hours with subsequent early hospital discharge (Hansen, 2007); 4) early postoperative oral intake seems to be superior to delayed intake by reducing time to first solid diet, presence of bowel sounds, and shorter hospital stay, at the expense of slightly increased nausea (Charoenkwan, 2007); 5) the combination of intravenous morphine with butorphanol reduces opioid requirements and some opioid-related side effects, but causes sedation, sweating and dry mouth (Wang, 2009); 6) the combination with nalbuphine, a mixed opioid agonist-antagonist, also seems to attenuate opioid-related nausea, but other opioid-related side effects remain unchanged (Yeh, 2009); 7) the omission of a background rate of infusion of morphine for intravenous patient-controlled analgesia (PCA) seems to reduce overall morphine consumption, reduce nausea, vomiting and dizziness but, again, other opioid-related side effects remain unchanged (Chen, 2011); 8) intravenous oxycodone seems to cause less opioid-related sedation than intravenous morphine, but other side effects are similar, suggesting a difference caused by stochastic variation (Lenz, 2009).

3.3 Gender-specific pharmacogenetics

Variations between opioids aside, even more pronounced differences may be found between individuals in terms of pharmacokinetics and, in particular, pharmacodynamics. In the past decade, research has given us a great amount of knowledge on the genetic disposition that explains these differences, and to what extent people react differently to pain. The opioid receptor and its determining gene (OPRM1) has been shown to have 17 variations (socalled polymorhism) that are unequally distributed between the sexes (Samer, 2010; Kolesnikov, 2011). Women are found to have µ receptor variations that predispose to longer clinical effects of an opioid, and twice as many side effects as men (Sarton, 2003; Niesters, 2010). In a study on A118G polymorphisms, patients homozygous for G118 required more morphine doses to achieve adequate pain relief compared with patients homozygous for A118 (Chou, 2006). Furthermore, the experience of pain may be unevenly distributed. Women experience more pain than men, and even among women major differences in the tolerance to each pain modality exist. Studies that address these variations suggest that at least six modalities may be identified (Lariviere, 2002; Hastie, 2005). The clinical relevance is enormous because several modalities of pain are at work following hysterectomy: nociceptive, ischaemic, pressure, temporal, neurogenic, chemical/irritative. The individual contribution of each pain modality may be difficult to assess in a particular patient, but each patient will react to certain pain sensations according to her particular sensitivity. Investigations into other postoperative complaints are also emerging and seem to share similar gender differences. These gender differences may include the actions of commonly used drugs for intraoperative sedation and pain relief, causing prolonged sedative effects and ill health in the post-anaesthesia care unit (Jensen, 2009).

4. Physiology

4.1 Physiological changes during surgery

Acute physiological changes during surgery are determined by the disposition and preoperative state of the patient, the type and depth of anaesthesia, and the surgical

technique. Important preoperative patient factors include heart and lung function, body mass index, metabolic disorders, concurrent medications or alcohol, and level of hydration; such factors determine the mechanistic vascular responses to surgery and the sensitivity to drugs, fluids and body positioning. Serious complications include hypotension, bradycardia, atelectasis, hypoxia and awareness, all of which may be adequately prevented and treated. Particular interest should be paid to surgical techniques involving laparoscopy. Pneumoperitoneum increases intraabdominal pressure and, either alone or with Trendelenburg positioning, may increase/decrease cardiac preload, increase cardiac afterload, reduce pulmonary volumes, decrease functional residual capacity and increase closing volume. This may lead to circulatory instability, atelectases and hypoxia (Strang, 2009; Hedenstierna, 2010). Oxygenation may be considerably improved by alveolar recruitment maneuvres and positive end-expiratory pressure, and these measures are considered mandatory for pulmonary protection (Park, 2009). The immune system seems resistant to most types of anaesthesia. Metabolic changes such as cortisol rise is more pronounced in vaginal than laparoscopic surgery, although stress response with catecholamine levels are high in both types of surgery (Lattermann, 2001). Laparotomy is associated with increased levels of C-reactive protein, creatine phosphokinase and lactic dehydrogenase compared to laparoscopic-assisted vaginal technique, corresponding to the greater amount of tissue damage inflicted; these immunological differences are in turn reflected in clinically useful measures such as length of stay (Atabekoglu, 2004). Although the clinical value remains controversial, preoperative epidural blockade may in fact attenuate interleukin levels associated with the inflammatory response after abdominal hysterectomy (Beilin, 2003).

4.2 Anaesthetic technique

The type of anaesthesia is highly variable between surgical centres and is in a limited way dictated by type of surgery. General anaesthesia is the preferred method, with supplemental epidural analgesia, perineural or infiltrative analgesia when major postoperative pain is anticipated. Spinal anaesthesia may be an alternative for abdominal or vaginal hysterectomy allowing for less postoperative morphine demands, but the use of intrathecal morphine also includes more postoperative itching (Sprung, 2006; Massicotte, 2009; Wodlin, 2011). Fast-track programmes using spinal anaesthesia with intrathecal morphine may even be associated with improved quality of life measures several weeks after surgery compared to general anaesthesia, because even minor complications adversely affect the mental component of quality of life and duration of sick leave (Ottesen, 2002; Penketh, 2007; Wodlin, 2011). General anaesthesia counteracts the cardiovascular effects of the physiological stress response by dilating peripheral vasculature, reducing cardiac output, blood pressure and heart rate in a dose-dependent fashion. Metabolic responses to surgery are, however, largely unaffected by sedative agents alone, and in order to suppress these responses as well, opioids or neuraxial anaesthesia should be used (Demirbilek, 2004; Hong, 2008; Ihn, 2009). Sedation is almost always combined with an efficient intraoperative opioid, and all opioids may in principle be adequate; controllability of dosage and effect is the primary concern for the clinician. Level of sleep may be estimated by bispectral index monitoring, although some controversy exists regarding the applicability and usefulness of its largely unknown algorithm for interpreting depth of anaesthesia (Meyhoff, 2009). Autonomic signs such as hypertension, tachycardia, pupil dilation, sweating and reflex

movement are useless for identifying patients that may be partially awake and at risk of awareness. A particular side effect of inhalational anaesthesia is the increased risk of postoperative nausea and vomiting (PONV), suggesting that intravenous drugs may be preferable. Propofol may in itself be antiemetic. The decision between inhalational anaesthesia and TIVA does, however, remain difficult. Studies comparing the two anaesthetic methods are equivocal, with a tendency towards superiority in the TIVA groups in terms of less nausea and earlier start of oral fluid intake (Fassoulaki, 2008; Kroon, 2010). A recent study suggests that deep levels of intraoperative sedation (as measured by auditory evoked potentials) may reduce postoperative morphine demands (Henneberg, 2005). It was conducted using TIVA, but it remains unknown if a similar relationship may be seen with inhalational agents. This would justify a more widespread use of monitoring devices for depth of sedation.

4.3 Epidural blockade as an adjuvant technique

The use of an adjuvant epidural has had strong support for many years. It reduces surgical stress response, reduces sedative requirements (Morley, 2002), shortens length of stay in the post-anaesthesia care unit (Jensen, 2009) and may serve as route of administration for other adjuvant drugs beside local anaesthetics and opioids. Duration or quality of analgesia has been shown to be increased by the addition of butorphanol (Bharti, 2009), magnesium (Farouk, 2008) or clonidine (Topcu, 2005). The combination of epidural local anaesthetics with opioids does however remain a basic requirement (Niiyama, 2005), and epidural opioids carry with them an increased risk of gastric paresis, obstipation, nausea and bladder paresis. Furthermore, while the use of an epidural may reduce pain and opioid demands, it seems to have only limited effects on gastrointestinal function and patient recovery (Jørgensen, 2001). In conclusion, the epidural technique has several shortcomings as an adjuvant technique and does not convincingly seem to solve the basic clinical problems in the immediate postoperative period.

4.4 Surgical technique

The type of surgery probably has the greatest impact on the physiological changes during surgery. Many of these are expected from a mechanistic point of view in relation to Trendelenburg positioning, increased abdominal pressure, variations in cardiac preload and afterload, positive pressure ventilation, fluid therapy and depth of anaesthesia, but some are also infrequent. They include hypothermia, deep vein thrombosis, cardiac arhythmias, circulatory collapse from sympathetic trunk block and metabolic changes during surgical stress response. The choice between surgical techniques is often made by the surgeon in conference with the patient, but the reasons are often unclear. From the view of an anaesthesiologist, only in the past few years do we have strong scientific support for the effect of surgical technique on postoperative complaints. It seems evident that a minimally invasive technique using laparoscopy and/or vaginal approach is superior to laparotomy, in terms of less postoperative pain, less morphine demand, shorter duration of bladder catheterisation, better immune function, length of stay in hospital, and measures of postoperative vitality (Ribeiro, 2003; Garry, 2004; Ghezzi, 2010; Naik, 2010). Minilaparotomy has similar advantages to ordinary laparotomy (Sharma, 2004). Laparoscopic technique seems superior to vaginal approach in terms of reduced postoperative pain and length of

stay in hospital (Candiani, 2009). Recent advances such as single-port-access laparoscopy techniques may reduce pain scores even further (Kim, 2010). The extent of surgery (subtotal vs total hysterectomy) does not seem to affect short-term or long-term recovery (Lethaby, 2006; Persson, 2010).

5. Pain and discomfort

5.1 Management of postoperative pain

A complete list of randomized trials investigating the analgesic value of pharmacological and psychological interventions in abdominal hysterectomy is available at the website by the Prospect Research Group (www.postoppain.org). The site covers the entire period 1966-2004, with additions into 2006 for some drugs, and a complete reference list is available. An extracted summary of the available procedure-specific evidence has been derived in Table 1, but caution should be observed in taking information at face value. With the advent of new, minimally invasive surgical techniques, thoughts about laparotomy procedures may be posthoc. It may only represent our abilities to attenuate problems caused by the most traumatic surgical technique possible, and it may not be up-to-date in regard to the spectrum of currently available analgesic techniques. This chapter therefore warrants some notes on developments in pain management that have taken place within the last few years.

Intervention	Preoperative	Intraoperative	Postoperative
Intravenous/oral opioids	0	2	2
Intravenous/oral NSAIDS or coxibs	0-1	2	2
Oral gapabentin or pregabalin	2	?	2
Oral/rectal/intravenous paracetamol	1	?	1
Intravenous tramadol	?	?	1
Intravenous ketamine	0	0-1	1
Epidural local anaesthetics	0-1	2	1-2
Epidural ketamine	0	1	?
Epidural opioids	2	0-2	2
Epidural clonidine	2	0-2	1-2
Spinal local anaesthetics	2	?	2
Spinal opioids	1-2	?	?
Wound infiltration with local anaesthetics	0-1	0-1	0-1
Intraperitoneal local anaesthetics	-	0	-
Cognitive treatment	2	0-1	?
Music	?	1	0
Acupuncture	1	0	1

Table 1. Summary effects of selected interventions on postoperative pain after abdominal hysterectomy according to the timing of administration. *Notes:* 0, no analgesic effect; 1, some analgesic effect; 2, considerable analgesic effect; ?, data not available; -, data irrelevant.

5.2 Extent of tissue trauma

The anatomical basis of pain following hysterectomy is complex. In chapter 2, we have outlined some psychological and neurophysiological aspects of importance, and highlighted

the importance of tissue trauma as the cornerstone of surgical stress response and subsequent activation of prostaglandins, cytokines, and nociceptive impulses for central nervous system modulation. These reactions are best known in the skin, in which a variety of vasoactive and irritative substances are released by tissue damage, causing a primary area of hypersensitivity, and a secondary activation of metabolites and nerve impulses in the spinal cord and central nervous system, in turn causing an additional hypersensitivity around the initial skin damage (Dirks, 2002). Brain centres value-set these painful impulses, affecting cognition, emotions, motor cortex and the autonomous nervous system. In the abdomen, the most pronounced effect during hysterectomy is activation of the vagus part of the autonomous nervous system, arising from stimulation of the neural tissue surrounding the uterus, leading to bradycardia, hypotension and nausea. Since the extent of cutaneous tissue damage during surgery determines the frame of postoperative pain complaints, the potential methods of prevention and treatment should mirror the desired clinical effect and the acceptability of side effects. In this respect, clinicians may judge inconsistently because priorities may vary according to specific demands afforded by the patient or the specific situation.

5.3 Weak analgesics

Tramadol is a weak opioid that has failed to convincingly show benefits (Wang, 2009). Intravenous paracetamol, a weak cyclooxygenase-inhibitor in the CNS, has gained interest in a recent study that implies an additional opioid-sparing effect when given preoperatively in abdominal hysterectomy (Arici, 2009). Rectal paracetamol, on the other hand, has almost no effect (Kvalsvik, 2003). As for NSAIDs and cox-2 inhibitors (which only differ in their side effect profiles and duration of action), many studies continue to be done by the pharmaceutical companies. New intravenous formulations given during surgery clearly confirm the almost ubiquitous opioid-sparing quality of these drugs, but they add nothing new to our spectrum of useful drugs, other than handy iv formulations. A much more interesting study using intrathecal ketorolac as adjuvant in patients with chronic or postoperative pain following vaginal hysterectomy showed that, while contributions of prostaglandins from the spinal cord must be evident in the development of pain, it is clearly only of value to block prostaglandin production (by ketorolac) if levels of prostaglandin E2 are high in the cerebrospinal fluid, an event which only occurs in a subset of patients. In addition, intrathecal ketorolac does not alter time to first morphine demand after surgery (Eisenach, 2010).

5.4 New drugs

Dexamethasone has been the focus of several studies, and when used alone in laparoscopic hysterectomy, it has clinically relevant opioid-sparing properties, as well as reducing the risk of dizziness (Jokela, 2009; Thangaswamy, 2010). When used in combination with pregabalin for abdominal hysterectomy, however, one study did not replicate these properties (Mathiesen, 2009), suggesting a potentially weak analgesic effect. It should also be noted that dexamethasone at 8 mg dose given before surgery causes significant hyperglycaemia within the first six postoperative hours (Eberhart, 2011). The value of gabapentin and pregabalin are confirmed in studies published after the Prospect review and may in fact also lead to faster recovery of bowel function (Turan, 2006; Durmus, 2007). The

combination of gabapentin and a cox-2 inhibitor seems to be superior to either single agent for postoperative pain, as well as improvements in mood and sleep quality (Gilron, 2005). For gabapentin, 1200 mg/day is the appropriate dosage, whereas for pregabalin it is 300 mg/day (Ittichaikulthol, 2009). When compared to ketamine (low dose infusion), gabapentin seems to improve pain scores, but either drug seems equally efficacious as opioid-sparing agents (Sen, 2009; Pirim, 2006). For gabapentin, side effects include dizziness and sedation, and for ketamine, side effects include sleep disorders, hallucinations and a condition known as "dissociative anaesthesia" (to feel present, yet distant; to feel pain, yet not to care). When used within proposed dose limits, these side effects are exceedingly rare. The alpha-2 antagonist dexmedetomidine may be used as a continuous infusion during surgery or as an effective adjuvant to iv PCA morphine after abdominal hysterectomy, decreasing pain levels without increasing the incidence of side effects such as sedation or hemodynamic instability (Gurbet, 2006; Lin, 2009). Intraoperative dexmedetomidine may also reduce the risk of postoperative shivering (Elvan, 2008). Other CNS-active drugs such as droperidol, cyclizine and promethazine reduce postoperative morphine consumption and the frequency of nausea and vomiting compared to placebo (Chia, 2004; Lo, 2005). The biologically active drug melatonin, which is used for circadian rhythms and sleep, has recently been highlighted in two interesting studies. When given as an oral dose of 5 mg the night before and one hour before surgery, it has reduced opioid requirements and postoperative anxiety, and patients regain their circadian rhythm more quickly after surgery (Caumo, 2007). Given the demonstration that melatonin has both analgesic, anti-inflammatory, and anxiolytic properties, and that higher anxiety makes the control of postoperative pain more difficult, one can hypothesize that melatonin is a promising agent to improve the control of postoperative pain. The efficacy of melatonin equals that of clonidine after abdominal hysterectomy (Caumo, 2009). Finally, intravenous lidocaine has both analgesic and antiinflammatory properties, which decrease the upregulation of proinflammatory cytokines, but clinical results have been disappointing (Yardeni, 2009; Bryson, 2010).

5.5 Acupuncture

Intraoperative use of acupuncture has been investigated and has been found to have no value in abdominal hysterectomy (Table 1). However, when applying classical needle acupuncture, electroacupuncture or capsicum plaster at certain acupoints (Zusanli, ST-36) preoperatively or postoperatively after abdominal hysterectomy, requests for morphine and antiemetics are significantly reduced (Lin, 2002; Kim, 2006; Grube, 2009). Other studies using electroacupuncture at 10 Hz have failed to confirm these findings, suggesting that acupuncture points need to be clearly defined and that the procedure itself requires special knowledge to perform (El-Rakshy, 2009).

5.6 Local anaesthetic techniques

The paradigm of blocking nerve conduction at the site of injury without the need for additional systemic analgesics is an enduring and very enticing proposition. While the need for such techniques are decidedly relevant in scenarios with considerable tissue damage such as conventional laparotomy, it seems appropriate to consider their use in laparoscopic surgery as well. The overall efficacy of local anaesthetic infiltration around the surgical

wound is not entirely convincing. The main problem is duration of action, which is usually only a few hours. Due to the enhanced blood flow caused by inflammation, instilled drugs are washed out very quickly. For this reason, continuous catheter solutions seem promising (Gomez Rios, 2009). The placement of the catheter, however, is important and must be situated above the fascia to have any effect (Hafizoglu, 2008; Perniola, 2009). The physiological reason is perfectly straightforward, since most pain-conducting nerves are located in this area.

5.7 Transverse Abdominis Plane (TAP) block

The administration of various forms of TAP blocks has attracted a substantial interest during the last decade. The emergence of anaesthetic ultrasound, the simplicity of the block and the rapid effect on postoperative pain following many abdominal procedures are among the primary movers for the widespread use of the TAP block (Petersen, 2010; Børglum, 2011, Koscielniak-Nielsen, 2011). The block has evolved from an abdominal wall block administered blindly and based on anatomical landmarks to an ultrasound guided block, where the spread of the injectate can be seen to be deposited in the right compartment; i.e. in the neurovascular plane between the internal oblique and the transversus abdominis muscles (Rafi, 2001; McDonnell, 2007; Petersen, 2010). Recently, the block has been refined and described in more detail when the aim of various studies was to expand and ensure the analgesic efficacy of the block to cover the entire abdominal wall (Th6-Th12(L1)) (Hebbard, 2010; Børglum, 2011). Most interestingly, the TAP block administered blindly prior to surgical incision for total abdominal hysterectomy using the double loss-of-resistance technique together with the traditional landmark assistance has been proven to provide superior analgesia when compared to a placebo group (Carney, 2008). Patients in the active group had reduced 48-h morphine requirements, and a longer time to first PCA morphine request. Postoperative VAS pain scores at rest and on movement were reduced after TAP block at most time points assessed (over 48 hours) (Carney, 2008). It would seem that promising results in this area could merit further studies. An internet search provided proof to this matter, since novel studies registered on ClinicalTrials.com exhibited research projects concerning laparoscopic vaginal hysterectomy and the efficacy of pre-operative TAP block on postoperative pain management. In addition, it would seem plausible that other types of truncal blocks such as ultrasound-guided thoracic paravertebral (TPV) blocks and rectus sheath blocks could well provide benefits in postoperative pain management following either abdominal or laparoscopic hysterectomy. Recently, TPV and rectus sheath blocks were given grade B and A recommendations for ultrasound guidance (United States Agency for health Care Policy and Research), respectively (Abrahams, 2010). An anatomically more caudal, but equally effective block option is bilateral ilioinguinal nerve block (Oriola, 2007). Thus, it seems straightforward to include any of these blocks in a multimodal analgesic regime.

5.8 Postoperative Nausea And Vomiting (PONV)

Nausea and vomiting rank high among feared postoperative complaints. Even to this day, they are also among the most common after any kind of hysterectomy. PONV may be caused by a variety of factors (Table 2). Commonly used algorithms for prevention should be taken as guidelines rather than statements of fact, because new techniques have changed

the foundation for the specific frequencies of PONV cited in the algorithms (Eberhart, 2000; Gan, 2007). Another methodological problem is frequency of PONV, which often differs considerably (0-80%) in comparable studies. The good part of the story is that PONV usually abates within 24 hours, but because of its frequency and enormous impact on well-being, clinicians must hold a strong focus on its prevention. While studies on PONV are heterogeneous, randomized data suggest that combinations of at least two antiemetics are effective for prophylaxis, reducing the risk of PONV to less than 20% (Piper, 2003; Chu, 2008). Antiemetics may also with advantage be added to patient-controlled analgesia infusions (Boonmak, 2007). The specific type of antiemetic is less important and should be guided by the desired effect and potential side effects (Bilgin, 2010). For instance, when PONV may be aggravated by anxiety, a benzodiazepine or sedative antiemetic is preferable (Elhakim, 2009; Fujii 2010; Huh, 2010). Antiemetics used for prophylaxis may also be used for treatment. Again, the use of acupuncture has reliably been shown to prevent PONV. Of special importance is the P6 point at the wrist (Frey, 2009; Kim, 2011). The Korean K-D2 or auricular points are equally useful (Ki, 2002; Kim, 2003).

DEFINITE risk factors for PONV

Females	Non-smokers
Previous PONV	Motion sickness
Opioids	Inhalational anaesthetics and N2O
Neostigmine	General anaesthesia
Prolonged surgery	

PRESUMED risk factors for PONV

Hormonal imbalance	Obesity
Pain	Anxiety
Early mobilization and transport	Laparoscopy

Table 2. Definite or presumed risk factors for PONV in females undergoing hysterectomy.

Benzodiazepines	Propofol	Chlorpromazine
Antihistamines	Droperidol, haloperidol	Metoclopramide
Dexamethasone	Serotonine antagonists	Ephedrine
Effective pain management	P6 acupressure	

Table 3. Modalities in prevention and treatment of PONV.

5.9 Development of chronic pain

Chronic pain is frequently observed several months after laparotomy (7 to 37%, depending on incision) (Perkins, 2000); the most apparent cause is direct nerve damage by severance or compression, leading to a host of nerve changes including peripheral receptor and spinal neuron changes, hyperalgesia/allodynia, ectopic activity and wind-up phenomena. Prevention is of key importance, since major breakthroughs in treatment have not yet emerged. In spite of an enormous amount of literature dealing with the prevention, pathophysiology and treatment of chronic pain, we are still at the very beginning of our understanding. Every effort should therefore be directed at minimally invasive surgical techniques. Persistent nerve damage resulting from epidural, spinal or regional anaesthesia is exceedingly rare and occurs in the order of 1:5000. Transient nerve damage (neuropraxia)

lasting weeks to months is more common following regional anaesthesia, but the incidence is largely unknown. Its pathophysiology also remains murky but may include compression or stretching effects of nerve fibres, toxic effects of local anaesthetic drugs, and an inherent increased susceptibility to compression effects (known as HNPP, hereditary liability to neuropathic pressure palsies). Patients having HNPP often complain of prolonged dys-aesthesias, wrist pain, and strange sensory sensations after even banal experiences. Nerve damage resulting from inadequate positioning during surgery in the lithotomy position, for instance, may be prevented by soft padding, frequent movement during surgery, and continuous monitoring of vascular supply by pulse oximetry. Brachial plexus damage may occur if arms are hyperextended from the axis of the body in steep Trendelenburg positioning (Ben-David, 1997).

6. Administrative logistics

6.1 Fast-track protocols

The concept of a fast-track surgical protocol for hysterectomy was introduced by Kehlet and associates a decade ago (Møller, 2001). The protocol included optimized information, well-defined anaesthesia and fluid therapy, early mobilization, early food intake and the concept of multimodal pain treatment. The idea was to combine several modalities of analgesic techniques, systemic to neuraxial, in order to harvest tbe benefits of synergistic effects. Using these concepts, the authors were even then able to optimize length of stay in abdominal hysterectomy to approximate that of laparoscopically-assisted vaginal hysterectomy, which strongly suggests that 1) the concept works, and that 2) benefits from randomized trials were until then not adequately transformed and utilized in clinical practice. Patients were simply not asked to get out of bed and take care of themselves, in spite of several well-meaning treatments and preventive measures that should facilitate ambulation and self-sufficiency. While the concept of fast-track protocols have continued to expand in recent years, there are however limits to the number of complaints that can be prevented by this paradigm. In a comprehensive cohort study looking at the immediate recovery profile after abdominal hysterectomy, several important points emerge (Jensen, 2009): 25% experience severe pain in spite of preoperatively placed epidurals, but only 8% experience PONV (patients were pretreated with three antiemetics). However, a complicated recovery, defined as the presence of severe complaints (pain or PONV), with more than five treatment interventions in the postanaesthesia care unit or a length of stay more than two hours, was observed in half the patients. The patency of the epidural was a key issue, and failed epidurals or patients not wishing/having epidurals were at particularly high risk of complaints. Inadequate pain treatment was the principal factor responsible for prolonged stay in the postanaesthesia care unit, causing increased opioid demands, nausea, dependency on oxygen supply, and sedation. Recent studies rightfully discuss the optimal surgical and anaesthetic techniques, but there are no clear answers (Sarmini, 2005; Abdelmonem, 2006; Wodlin, 2011). Spinal anaesthesia has some advantages to general anaesthesia by reducing immediate postoperative discomfort, opioid demands and duration of sick leave, but spinal opioids increase the risk of itching, with no differences in PONV (Wodlin, 2011a; Wodlin, 2011b). A similar fast-track study seems to imply that total intravenous anaesthesia may be superior to inhalational anaesthesia by reducing nausea, length of hospital stay, and duration of an indwelling urinary catheter (Kroon,

2010). The case for early urinary catheter removal, however, is offset by an increased risk of urinary retention episodes requiring re-catheterisation (Chai, 2011).

6.2 The economics of hysterectomy

Hot on the heels of the fast-track protocols, hospital administrators have become aware of the potential to reap the benefits of this new paradigm. Optimal logistics in the surgical suite, short durations of surgery, few necessary interventions or short length of stay in the postanaesthesia care unit are pivotal issues for increasing the number of surgeries that can be performed in a day. In the surgical ward, severity of activity-limiting and treatment-necessary complaints determine, besides surgical complications, the degree of observation and the level of competency that needs to be present, and ultimately the length of hospital stay. This length of stay in turn determines which days elective patients can be scheduled for surgery (typically monday through wednesday), so that only residual problems persist in the weekend and a clean slate of patients can be admitted the following monday (Roumm, 2005). Day surgery may be placed in the extreme end of the spectrum, facilitating quick patient flow, fewer overnight beds and lower costs (Levy, 2005), while complicated (acute, laparotomic) surgery may be placed in the other end. From the administrative point, the balance between the two extremes is as delicate as a double-edged sword: day surgery may reduce costs per patient, but increasing number of patients puts considerable pressure on optimized flow, well-functioning protocols, teamwork, the implementation of lean principles, patient profiles (ASA health status 1-2), and staff enthusiasm. Complicated cases puts pressure on staff competency, individual solutions and across-department collaborations. It is for these very reasons that medical technology assessments are important in determining the true logistical value of new anaesthetic or surgical techniques, because each new intervention affects the entire system of people and work descriptions in the surgical food chain. Studies investigating financial costs, e.g. the introduction of robotic surgery, should not uncritically be taken at face value: they often fail to take these issues into account and merely represent fictive scenarios that may or may not be applicable (Barnett, 2010; Oehler, 2011). In a wider perspective, the cost for the society may not be reflected in the immediate hospital costs. A recent study suggests that the majority of women extend their sick leave beyond the recommended period on their own initiative, despite the ward's long recommended period of sick leave (Johansen, 2008).

7. Conclusions

From the topics discussed above, several unmet patient needs and clear avenues of research still need to be pursued; even though multimodal, evidence-based treatment regimens are conducted efficiently and in detail, many patients still suffer from unacceptable postoperative complaints. The reasons are complex and include definite limitations in the current potentials of anaesthesia and surgery, stress response, variability among patients in psychological or genetic disposition, and downright treatment failures or withdrawals because of unacceptable side effects. Certain surgical techniques are related to more complaints. Pharmacologically, new drugs have not lived up to their potential to facilitate opioid-free analgesia. Recent advances in local anaesthetic techniques such as the transverse abdominis plane block may help solve this problem, but we are still in want of a magic bullet to alleviate nausea, dizziness, exhaustion and failed ambulation. From a patient perspective,

there is a need for adequate information to properly balance expectations and coping strategies, and a need for focused postoperative follow-up, since people are nowadays discharged early with health complaints and limitations in activities of daily living persisting for weeks or even months after surgery. A useful method for transferring procedure-specific evidence from controlled studies into the very real and heterogeneous world of uncontrolled patients and health care professionals is also highly welcomed. Can we succeed in this? Only the future will tell.

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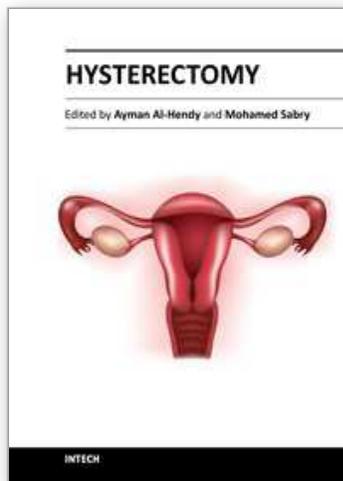
Hysterectomy

Edited by Dr. Ayman Al-Hendy

This book is intended for the general and family practitioners, as well as for gynecologists, specialists in gynecological surgery, general surgeons, urologists and all other surgical specialists that perform procedures in or around the female pelvis, in addition to intensives and all other specialities and health care professionals who care for women before, during or after hysterectomy. The aim of this book is to review the recent achievements of the research community regarding the field of gynecologic surgery and hysterectomy as well as highlight future directions and where this field is heading. While no single volume can adequately cover the diversity of issues and facets in relation to such a common and important procedure such as hysterectomy, this book will attempt to address the pivotal topics especially in regards to safety, risk management as well as pre- and post-operative care.

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