ANALGESIA AFTER SURGERY FOR BREAST TUMOR

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Summary

The choice of appropriate premedication and anesthetic technique may contribute to better postoperative analgesia. Intensity, frequency of occurrence, quality and duration of pain differ regarding the type of surgery: extent, site and duration of surgical procedure. They also depend on the patient's psychological profile, his perioperative psychological and physiological adaptation and the quality of postoperative procedures. Pain after mastectomy and evacuation of axillary lymph nodes is classified as moderate in nearly half of the patients, however, 10-30% of them may experience severe pain. In the management of postoperative pain, opioid and nonopiod analgesics are used. Poorly treated pain after surgery may be considered a significant factor for increased morbidity and mortality resulting in a protracted hospital stay and, subsequently, increased treatment costs. The intensity of chronic pain, that might occur in a form of phatnom pain in the chest, shoulder and upper arm region following breast surgery, greatly depends on good surgical technique, successful management of acute postoperative pain, and well-performed radiotherapy, chemotherapy and physical therapy. Prolonged pain with adverse effects on the respiratory, cardiocirculatory and neuroendocrine function, may lead to psychological disorders, i.e. depression, and produce long-term effects in the central and peripheral nervous system. Pain therapy should therefore be included in a so-called multimodal concept of postoperative rehabilitation.

KEY WORDS: *analgesia, breast tumor*

ANALGEZIJA NAKON OPERACIJA TUMORA DOJKE

Sažetak

Anesteziolog izborom premedikacije i anesteziološke tehnike može pridonijeti boljoj poslijeoperacijskoj analgeziji. Intenzitet, učestalost, kvaliteta i trajanje boli razlikuju se s obzirom na vrstu kirurškog zahvata: opseg, mjesto i trajanje operacije. Ovise također i o psihološkom profilu bolesnika, perioperacijskoj psihološkoj i fiziološkoj pripremi bolesnika, te o kvaliteti poslijeoperacijskih postupaka. Bol nakon mastektomije i evakuacije pazušnih limfnih čvorova u otprilike polovine bolesnika po jačini se ubraja u umjerenu bol, međutim, 10–30% bolesnika je doživljava kao jaku bol. U liječenju poslijeoperacijske boli upotrebljavaju se opioidni i neopioidni analgetici. Loše liječena poslijeoperacijska bol može se smatrati znakovitim čimbenikom povećanog morbiditeta i mortaliteta, koji rezultira produženim boravkom u bolnici i posljedično povećanim troškovima liječenja. Intenzitet kronične boli, koja se može pojaviti i u obliku fantomske boli u području prsnog koša, ramena i nadlaktice nakon operacije dojke ovisi o dobroj operacijskoj tehnici, uspjehu liječenja akutne poslijeoperacijske boli, dobro provedenoj radioterapiji, kemoterapiji i fizikalnoj terapiji. Prolongirana bol ima štetne posljedice na respiratornu, kardiocirkulatornu i neuroendokrinu funkciju, može dovesti do psihičkih poremećaje u smislu depresije, te izazvati dugotrajne posljedice u središnjem i perifernom živčanom sustavu. Terapija boli mora biti ugrađena u tzv. multimodalni koncept poslijeoperacijske rehabilitacije.

KLJUČNE RIJEČI: *analgezija, tumor dojke*

INTRODUCTION

Proper planning for breast cancer surgery requires careful evaluation of patient's psychological profile, finding out how much the patient knows about his disease, whether he is aware of the necessity of surgical treatment and is he psychologically ready for it. The patient may change

psychologically for fear of the disease itself, its prognosis and mutilation from the procedure. Fear itself leads to increased irritability of the nervous system, raises the possibility of complications during both anesthesia and the early postoperative period, decreases the pain treshold. By chosing appropriate premedication and anesthetic technique, the anesthesiologist may contribute to better postoperative analgesia.

During any surgical procedure, tissue trauma occurs resulting in sensitization of peripheral nociceptors. At the site of lesion, an inflammatory reaction develops. In the course of the inflammatory process, a complex neuro-immune interaction results in primary hyperalgesia. Prostaglandins and bradykinine are released as a result of cellular break-up. The release of inflammatory mediators from tissues, immune cells, sympathetic and sensory afferent nerve fibres results in an «inflammatory soup» both bathing the nociceptors and activating them directly or indirectly. The inflammation associated with hyperemia results in the further development of pain-causing mediators: nitric monoxide (NO) and the precoursor of bradykinine. Primary afferent neurons release neuropeptides that may cause sensitization. Immune cells also release proalgesic (neutrophin, cytokines, serotonine and histamine) and antialgesic molecules (opioids and cannabinoids). For sensitizating effects of prostaglandine, a functional activity of the sympathetic nervous system is required (1, 2).

The International Association for the Study of Pain has defined pain «as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage».

Pain is considered the fifth vital sign, along with puls, arterial pressure, core temperature and respiration frequency. The most common form of acute pain is postsurgical pain. It's a complex interaction of patient's subjective, emotional and psychological response. There is a large interindividual variability in patient's response to pain, and each person responds differently, depending on the circumstances.

Intensity, frequency of occurrence, quality and duration of pain differ regarding the type of surgery, extent, site and duration of surgical procedure. They also depend on the patient's psychological profile, his perioperative psychological and physiological adaptation and the quality of postoperative procedures. The operation site is considered the most important factor conditioning the intensity of postoperative pain.

Pain after mastectomy and evacuation of axillary lymph nodes is classified as moderate in nearly half of the patients, however, 10-30% of them may experience it as severe pain. Patients with properly treated pain feel comfortable and are easier to mobilize after surery, representing prophylaxis against deep vein trhmbosis and pneumonia, and they have decreased sympathetic tone, reduced myocardial oxygen consumption, better immunity and more stable metabolism. Both the choice of analgesia and the choice of its administration start in individual patients are fundamental determinants of the quality of treatment (3).

Pain is a personal experience, which makes it difficult to define and measure. It combines sensory input, modulation of physiological and psychological factors and factors of the patient's environment. Since there is no objective method of assessing pain, we should trust patients and rely on their self-report of pain. Measurement and documentation pave the way for appropriate pain management. The simplest techniques for pain assessment are visual analogue (VAS) and verbal rating (VRS) scales. VAS is widely employed in the assessment of postoperative pain. Which of the scales is to be used in practice remains relatively unimportant since they correlate well with each other (4).

In the management of postoperative pain both opioid and non-opioid analgesics are used.

Opioid analgesics

Opioid anagelsics are the most effective class of drugs for the management of acute pain. They are efficacious for both somatic and visceral pain of all intensities, from mild to agonizing. Strong opioid-induced analgesia in acute pain is explained by activation of the endogenous opioid system which is the main inhibitory mechanism of the physiological modulation of accute nociceptive transmission. They bind to specific opioid receptors. The three major types of opioid receptors are named μ, δ and κ. They

are distributed throughout the spinal cord and the central nervous system. Opioids are considered to cause hyperpolarization and reduction of the excitability of certain neurons by opening of potassium and closing of calcium channels. They also inhibit the release of various excitation neurotransmitters, such as glutamate and substance P.

Among strong opioid analgesics, morphine is the most frequently used opioid in cancer pain management administered as a bolus of 0.05-0.1 mg/kg t.t. i.v. or infusion of 0.01-0.03 mg/kg t.t./h. Of weak opioid drugs, tramadol is administered as a bolus of 0.5-1.0 mg/kg t.t. or infusion 0.25 mg/kg t.t./h (5).

Non-opioid analgesics

The most often used non-opioid drugs for postoperative analgesia include metamisol, paracetamol and non-steroid antirheumatic drugs.

Non-steroid antirheumatics (NSAR) have an anti-inflammatory effect by inhibiting the synthesis of prostaglandins that are present in many tissues, especially at the site of injury. Regardless of the route and mode of delivery (peroral, rectal or parenteral administration), they may lead to erosions and ulceration of the gastrointestinal mucosa. NSARs block the enzyme prostaglandin synthetase (cyclooxygenase) in the arachidonic acid cycle. Cyclooxygenase (COX) occurs in several isomeric forms. Three forms are known, and of them two isomers are well investigated. COX-1 is a constitutional enzyme occurring in almost all tissues, and mostly expressed in blood vessel walls, gastric mucosa and kidney. It plays a role in conversion of arachidonic acid (found in cellular membrane phospholipids) into a protective prostaglandin and thromboxane. COX-2 is an inducible isomere occurring in inflammatory tissues when cells are exposed to inflammation mediators. It catalyses the synthesis of prostaglandins responsible for modulation of the inflammatory reaction, nociception and hyperalgesia at the tissue damage site. The majority of NSARs comparably, nonselectively inhibit COX-1 and COX-2. Due to a significant role prostaglandins play in physiological functions (maintenance of gastric mucosal integrity, regulation of kidney blood flow), inhibition of prostaglandin synthesis accounts for the side-effects of NSARs. NSARs, such as ibuprophen, ketoprophen and diclophenac inhibit both isoform cyclooxygenases. Their therapeutic effects are mainly based upon the repression of inducible COX-2 activity, their side-effects resulting from inhibition of COX-1 (6).

So-called *coxibs* are newer COX-2-specific inhibitors. Their therapeutic doses inhibit only the COX-2 isoform. The first pharmacological agents among coxibs are celecoxib and refocoxib. Their therapeutic effect is comparable to a classic NSAR, only with less gastrointestinal side-effects. Taking into consideration relatively limited experience with the administration of coxibs compared to vast experience with the long-term administration of classic NSARs, their definite place in pain therapy has yet to be determined. Coxibs are referred to as the drugs of choice for the management of pain in patients with anamnesis of active ulcer and gastrointestinal bleeding.

In addition to NSARs, spasmolitic activity of metamisol or other spasmolitic agents are also used in the management of acute pain, as they may improve analgesic efficacy.

Non-opioid analgesics are primarily indicated in the treatment of pain after minor surgical procedures, and combined with opioid analgesics in major surgery. Potential side-effects can be prevented by careful choice of analgesics, administration of an appropriate dose and careful control of the patient.

The necessity of analgesics and their consumption are influenced by many factors. In the elderly, lower doses are required. Abuse of various substances or disruption of their use, hyperthyreodism, anxiety and affective disorders, liver and kidney damage, as well as various culture factors also change the need of analgesics. Some patients may be intolerate to any discomfort, and some display surprising self-control or even consider pain a constituent element of life (7).

Poorly treated postoperative pain may be considered a significant factor for increased morbidity and mortality resulting in a protracted hospital stay and, subsequently, increased treatment costs. The intensity of chronic pain, that might occur in a form of phatnom pain in the

chest, shoulder and upper arm region following breast surgery, greatly depends on good surgical technique, successful management of acute postoperative pain, and well-performed radiotherapy, chemotherapy and physical therapy. Prolonged pain with adverse effects on the respiratory, cardiocirculatory and neuroendocrine function, may lead to psychological disorders, i.e. depression, and produce long-term effects in the central and peripheral nervous system (8,9).

Pain therapy should be integrated in the so-called multimodal concept of postoperative rehabilitation, in which early mobilization and early eneteral nutrition play a key role.

Postoperative pain management after breast surgery

After breast surgery, 35-50% of patients experience moderate pain, while in 10-30% of them severe postoperative pain occurs. Pain lasts one to three days.

Reasonable treatment of pain in the intensive care nit includes intravenous administration of opioids, while their intramuscular administration is not recommended for various reasons. Intramuscular injections are painful, drug reabsorption and its blood and tissue levels are variable, and the analgesic effect subsequently unpredictable. Repeated intravenous injections or continuous intravenous opiod infusion delivered by an infusomate are usual routes of opiod administration in the intensive care unit. By repeated i.v. delivery of opioids a good analgesic effect can be obtained. However in the early postoperative course, continuous infusion should be prefered. A steady blood drug concentration level can thus be better maintained and variations of analgesic levels avoided. The dose of analgesic should be carefully titrated and the infusion speed adjusted. Once a dynamic balance is achieved, the dose should be reduced.

New techniques: PCA (patient-controlled analgesia) and EA (epidural analgesia) can significatly improve the treatment of postoperative pain.

PCA implies the active participation of patients in the analgesia implementation and it is an appropriate way to improve the quality of analgesia in the intensive care unit. The technique represents a model of intermittent i.v. administration of analgesics accommodated to the patient's request. Both the individual dose size and the minimum time interval between the doses are determined in advance. This technique meets requirements of individual patients, and may be applied to both epidural and interthecal administration of opioids. It requires an adequate microprocessor-controlled pump. *Epidural analgesia* also plays a significant role in the management of postoperative pain. Epidural analgesia implies the administration of opioids and/or local anesthetics through an epidural catheter. Drugs may be applied either continuously or intermittently. Patients with coagulation factor deficiencies and malfunction are at high risk for placement of an epidural catheter.

Intercostal nerve block can relieve pain after radical mastectomy. Each intercostal nerve provide branches for motor innervation of intercostal muscles, and lateral and anterior branches for sensory innervation of the chest and abdominal skin. Intercostal nerve block may be applied to any part of their pathway, and should be performed proximally to the innervation region to be anesthesized. In clinical practice, the block is most frequently performed dorsally in the costal arch region, or in the axillary line. In addition to postoperative pain relief, intercostal blockade improves breathing, coughing and expectoration, performance of physical therapy and alike (10,11).

In the University Hospital for Tumors, the opioid analgesic tramadol is most frequently used in the management of pain after breast surgery. It is delivered intravenously, either in continuous infusion or in signle i.v. doses. It is often combined with the non-opiod analgesic metamisol or non-steroid anti-rheumatics. Tramadol meets our requirements of good analgesia for postoperative pain. Neither significant effects to the respiratory and cardiovascular system nor increased frequency of nausea and vomiting have been observed (12).

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