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PREVENTION OF POSTOPERATIVE PAIN

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ПРЕДУПРЕЖДЕНИЕ ПОСЛЕОПЕРАЦИОННОЙ БОЛИ

Патрик Уолл в редакционной статье “Pain” в 1988 г. с воодушевлением рассматривал концепцию упреждающей аналгезии по предотвращению послеоперационной боли аналгетиками, применявшимися до операции. Фактически, идея предотвращения хирургической боли была предложена Crile в “Lancet” в 1913 г., и многие анестезиологи использовали этот принцип, давая морфин или петидин в премедикации. Многие испытания, проведенные без адекватной методологии, дали сопоставимые результаты. Kissin в 1996 г. заметил, что последствия не всегда очевидны, а реальность довольно разочаровывает. В последнее время несколько метаанализов, основанных на публикациях по правильной методике и применению новых лекарств, особенно ингибиторов NDMA-рецепторов (декстрометорфан, кетамин) и ингибиторов, зависимых от напряжения кальциевых каналов (габапентин, прегабалин), открыли новые горизонты.

Ключевые слова: боль, NDMA-рецепторы, премедикация.

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Patrick Wall in an Editorial of Pain in 1988 was extremely enthusiastic with the concept of pre-emptive analgesia, corresponding to the prevention of postoperative pain by analgesics used before surgery. In fact, the prevention of surgical pain is an old idea, already proposed by Crile in the Lancet in 1913, and many anaesthesiologists were utilising this principle giving morphine or pethidine in premedication. Many trials performed without adequate methodology brought contrasted results. Kissin in 1996, observed that the effects were not always obvious and the reality rather disappointing. Recently, several meta-analysis, based upon publications according to a correct methodology and introducing new drugs especially NDMA receptors inhibitors (dextrometorphan, ketamine) and inhibitors of voltage-dependant calcium channels (gabapentin, pregabalin) have opened new horizons.

Key words: pain, NDMA-receptors, premedication.

Physiological Bases of Prevention of Postoperative Pain

Surgical pain is mainly the result of an hyperalgesia and allodynia. Compared to a standard aggression, surgical pain is characterized by an hyperalgesia produced by noxious stimuli and allodynia by innocuous stimuli. Hyperalgesia is the result of a peripheral, or primary, and central, or secondary sensitization. In periphery the tissue injury produces the release from the blood cells (macrophages, polynuclears, mast cells and platelets) of a great number of mediators, the same involved in the inflammatory reaction

(bradykinin, prostaglandin, histamine, serotonine, cytokin). These substances are responsible for a vasodilatation of capillaries producing an edema and activating the release of inflammatory mediators. Theses mediators act also on the sympathetic nerves and on the end terminal or nociceptive fibers Aδ and C to produce the nociceptive input, but also to release some substances such as the substance P, the CGRP and the nitric oxide (NO) which act on the blood cells creating a feed back mechanism and on the tissues surrounding the lesion to extend the area of hyperalgesia allodynia. The measurement of the area of hyperalgesia by a Von Frei's filament around the skin incision is an appropriate method to assess the efficiency of the prevention of hyperalgesia extension.

The Aδ and polymodal C fibers constitute the presynaptic neurones bringing the nociceptive input from the periphery to the dorsal horn of the medulla. At this level the transmission of the nociceptive input is made accross a synapse to the neurones of ascending pathways. A modulation of the transmission takes place in the dorsal horn due to a great number of synapses with neurones coming from the periphery transmitting the tactile sensitivity (fibersAα) — sensitive afferentations-, bulbospinal descending inhibiting pathways 5 HT and norepinephrine as mediators, interneurones releasing CCK, GABA, enkephalins, dynorphin, astrocytes and glial cells. All these substances released in the synaptic gap will modulate the transmission of the nociceptive Input by fixation on their specific receptors lying on the cell membranes of the pre and post synaptic neurones.

The transmission of the nociceptive input is mainly due to the release of glutamate from the presynaptic neurone in the synaptic gap and the fixation on the NMDA receptor on the post synaptic neurone.

The NMDA receptors are at the level of the post synaptic neurone membrane, linked to ions channels. The fixation of glutamate on the NMDA receptor moves the magnesium (Mg^2) blocking the ion channel and allows the entry of calcium (Ca^2) and sodium (Na) within the postsynaptic neurone modifying its polarity and activating the enzymatic systems. Conversely, NMDA blockers, like ketamine, are able to suppress the permeability of the ions channels and to avoid the activation of the postsynaptic neurone and the transmission of the nociceptive input.

In the dorsal horn, the modulation of the nociception may be due to physiological mechanism, implying the release of a great number of mediators and their fixation on their specific receptors, but also to pharmacological mechanisms such as the fixation of opioids on the pre and post synaptic opioid receptors. This pharmacological control may be obtained also by the NMDA receptors blockers such as dextromorphan and ketamine, and by a blocker of the voltage-dependant channels, the gabapentin.

Opiods can elicit an increased sensitivity to noxious stimuli due to an opioid induced hyperalgesia [5; 6] producing an acute tolerance to opioids. The fixation of opioids to mu-receptors can produce an inhibition of the nociceptive transmission producing a short-term analgesia. In the same time, the opioids can stimulate the phosphokinase C and activate NMDA receptors producing the entry of calcium within the post synaptic neurone constituting a facilitating system of nociception, responsible for hyperalgesia and allodynia on the long term.

The NMDA receptor blockers, dextromorphan and ketamine, could potentiate opioids by their own analgesic effects and by inhibition of the opioids acute tolerance.

A recent publication of Wilder–Smith Ohg and Arendt–Nielsen L. [7] underlines several mechanisms possible implying a central sensitization, a descending facilitation and a direct hyperalgesic action by fixation on the mu-receptor, but also a facilitation of the excitatory effect through the GS-coupled mu-opioid receptor and an antiglycinergic action.

Prevention of the postoperative hyperalgesia

To achieve successful preemptive analgesia, critical principles must be observed. Analgesia must be enough:

— deep, to block completely the nociceptive process;

— wide, to cover the entire surgical area;

— prolonged, to last throughout surgery including the pre and postoperative period.

Several meta analysis have recently demonstrated the interest of preemptive analgesia. Based upon three combined outcomes: reduction of pain scores, analgesic consumption and delay to request rescue analgesic, ONG CKS et al. [8] have retained 66 publications, gathering 3261 patients. The best efficiency is obtained with epidural analgesia, followed by the infiltration of local anaesthetics and parenteral AINS. Opioids and NMDA receptors blockers had a smaller level of proof.

Nevertheless, many publications and several very recent meta-analysis demonstrate clearly the role of ketamine ant dextromorphan. The classical publication by Stubhaug A. et al. [9] emphazises the conditions for an efficient use of ketamine: a dosis started before surgery and an infusion of small doses during surgery continued until 48 hours after surgery. These data have been confirmed by the publications of Argiriadou et al. [10] demonstrating a lack of statitistical significance between a single dose of ketamine and a placebo, and conversely a significant difference between repeated doses versus a single dose in term of VAS score and rescue dosis of diclofenac consumption. The Mc Cartney et al. meta-analysis [4] shows clear preventive effects of dextromorphan and ketamine but failed to demonstrate an efficacy of magnesium. An other meta-analysis by Elia and Tramer [11] based upon 53 randomised trials, 2839 patients, according to Oxford criteria of validity, confirms a reduction of pain scores, of cumulative morphine consumption and a low incidence of ketamine related adverse effects.

Similar results have been observed with a unique preoperative oral gabapentin dose of 1200 mg which decreases pain score, opioid consumption and morphine associated side effects. Turan et al. in spinal surgery [12] and in post hysterectomy pain [13] have demonstrated a statisticaly significant decrease respectively in morphine and tramadol consumption in patients receiving oral gabapentin 1200 mg, one hour before surgery.

In a more recent publication, Turan et al. [14] have modified the protocol, adding the same dose of gabapentin 24 and 48 hours after surgery. These data have been confirmed by several publications [15] but a sufficient dose of gabapentin seems necessary to be efficient [16]. The combination with a COX2 inhibitor, such rofecoxib, is superior to either single agent [17] and could be considered in favour of the balanced analgesia.

A New Challenge for Preemptive Analgesia: the Control of Chronic Neuropathic Surgical Pain

Postoperative chronic pain can correspond to various mechanisms: deafferentation, such as the phantom limb pain, causalgia, with complex regional pain syndromes, but more frequently, pain associated with tissue and nerve lesions. These chronic neuropathic postoperative pains are often underestimated due to a lack of long-term follow-up of the patients by the anaesthesiologist.

A systematic clinical assessment is necessary several months after surgery. Until now, few trials have demonstrated a possible reduction of secondary hyperalgesia, and the only publication from De Kock et al. [18] has emphazised a positive effect of spinal clonidine at six months. The chronic post surgical neuropathic pain seems frequent mainly in thoracic surgery and mastectomy, but also is many other frequent surgical processes such as

cholecystectomy, herniorraphy, abdominoperineal resection, vasectomy, menisectomy... Recent publications of Kehlet et al. [19] precise the risk faction and prevention of persistent post surgical pain.

Additional investigations on the epidemiology of the post surgical persistent pain in various types of surgery are necessary to evaluate more accurately the incidence evaluated to 10–50% of the patients, with severe chronic pain in about 2.10% of these patients. A simplified questionnaire (DN4) proposed by Bouhaissira et al. [20] should be useful to make a screening of the patients during the months and years following surgery. This important entity of chronic pain needs more investigations for identification of patients at risk, for diagnostic of persistent pain and for multimodal pharmacological treatment and prevention.

Prevention of postoperative pain has a long background, a strong evidence for theoretical support and a wide field of development with mechanisms based therapies.

Ключові слова: біль, NDMA-рецептори, премедикація.

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ULTRASOUND-GUIDANCE LUMBAR SYMPATHETIC GANGLION BLOCK. CASE REPORT

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РУКОВОДСТВО ДЛЯ ПОЯСНИЧНОГО СИМПАТИЧЕСКОГО БЛОКА ПОД УЛЬТРАЗВУКОВЫМ КОНТРОЛЕМ. КЛИНИЧЕСКИЙ СЛУЧАЙ

Блок поясничного симпатического ганглия (LSGB) относится к одному из инвазивных методов, который используется в лечении хронической боли, а также в других ситуациях. Этот тип блока выполняется с помощью флороскопии.