UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA
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ABSTRACT

DOCTORAL THESIS

ANALGESIA AN IMPORTANT ELEMENT IN THE POSTOPERATIVE MANAGEMENT OF THE PATIENT. MULTIMODAL ANALGESIA AS AN ADDITIONAL ANTINOCICEPTIVE METHOD

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INTRODUCTION

Adequate control of the postoperative pain plays an important role in perioperative management, taking into account the fact that, beyond the fear for the outcome of surgery, the main concern of patients is related to postoperative pain’s intensity, which is often perceived as the most unpleasant event of the surgical act. Thus, the main objective of the therapy is to maintain postoperative quality of life and rapid postoperative recovery. Surgical pain is a particular form of acute pain that occurs in response to tissue damage caused by the surgical act, and it is the expression of autonomic responses, that can produce an unpleasant and unwanted sensory-emotional experience.

Side effects that may occur due to inadequate treatment of acute pain in the perioperative period include thromboembolic or pulmonary complications and impaired quality of life. Surgical tissue damage can cause long-term alteration of central processing of spinal nociceptive information, and this fact can cause hyperalgesia. This can induce amplification and prolongation of postoperative pain.

The purpose of the present research was to analyze the incidence of acute postoperative pain and its impact on patients prognosis, and to identify methods of prevention and treatment of acute pain. I assessed both traditional pain relievers methods, and modern methods, as preemptive analgesia and multimodal analgesia.

This thesis is divided into two main parts: the first part is presenting the current state of knowledge in acute postoperative pain and the second is presenting the personal research data.
I. STATE OF KNOWLEDGE

1. PAIN. DEFINITIONS AND CLASSIFICATIONS

There are numerous different definitions for pain. The most widely accepted definition of pain is the one used by The International Association for the Study of Pain. It defines pain as “An unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage”.

Different classification systems were used depending on the duration of pain and clinical features.

2. NEURO-ANATOMY STRUCTURES OF PAIN.

PATHOPHYSIOLOGY OF PAIN

In this chapter are described the neuroanatomy structures of pain from the classification of nociceptors to pain pathway and central pain mechanisms.

Most of the pain fibres enter in the dorsal root of the spinal cord (the "sensory" root) and then synapsed in the dorsal part of the spinal grey matter, before passing the message up through the spinothalamic tract. These spinothalamic fibres have extensive connections throughout the brainstem and from there project to the medial thalamus and the cortex.

As important as the ascending pathways, are descending pathways that modulate the incoming signal. These are predominantly noradrenergic and serotonergic, and can be modulated by stimulation of opiate receptors.

3. QUANTITATIVE AND QUALITATIVE EVALUATION OF POSTOPERATIVE PAIN

Several pain intensity scales are currently used to assess the pain, such as visual analog scales, numeric rating scales, faces pain scale, McGill’s questionnaire etc.

The most used is the Visual Analog Scales. VAS is usually a horizontal line, 100 mm in length. The patient is asked to mark on the line his/her perceived pain intensity. The VAS score is determined by measuring in millimetres from the left hand end of the line to the point that the patient marks.
4. DRUGS USED IN PAIN THERAPY

In this chapter are described the main classes of drugs used in pain therapy: opioid medications, nonsteroidal anti-inflammatory drugs and adjuvant analgesics.

Adjuvant analgesics are defined as drugs with a primary indication other than pain that have analgesic properties in some painful conditions. The group includes numerous drugs in diverse classes, such as the tricyclic antidepressants, anticonvulsants, N-methyl-D-aspartic acid receptor antagonists, low-dose intravenous local anesthetics etc. Such agents are often administered in cases of refractory pain. For some chronic pain syndromes, however, they may constitute a first-line approach.

There are also presented new therapeutic target with analgesic properties such as: cannabinoid receptors, neuronal nicotinic receptors, glutamate receptors, P2X3 receptors purinergici, calcium channel neural type N.

5. ACUTE POSTOPERATIVE PAIN

Acute pain is generally accepted as being of recent onset and limited short duration. It usually has a temporal (follows immediately after surgery/trauma) and causal (has a known cause) relationship to injury or disease. The intensity of acute pain is greatest at the onset of injury but with healing pain intensity reduces.

The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain, and reduced cost of care.

6. PERIOPERATIVE TECHNIQUES FOR PAIN MANAGEMENT

In this chapter are described some of the most important perioperative techniques for pain management: PCA with systemic opioids, epidural or intrathecal opioid analgesia, regional analgesic techniques, including but not limited to plexus blocks, and local anesthetic infiltration of incisions.

Also in this part are described modern treatment methods like preemptive analgesia and multimodal analgesia, the last involving associations of different analgesia
techniques and analgesics with different mechanisms of action, for providing superior analgesic efficacy with equivalent or reduced adverse effects.

II. PERSONAL RESEARCH

The personal research includes four clinical studies:

7. ANALYSIS OF ACUTE POSTOPERATIVE PAIN. THE IMPACT, TREATMENT AND CONSEQUENCES OF PAIN IN A GROUP OF POSTOPERATIVE PATIENTS ADMITTED IN AN INTENSIVE CARE UNIT.

Wishing to improve the quality of analgesia, and to anticipate and eliminate unacceptable levels of pain, the first study examines the impact and consequences of acute pain secondary to surgery, on a group of 245 patients admitted in intensive care unit after surgery.

Present research shows that despite a sustained antinociceptive therapies, respecting the analgesia scale of World Health Organization, there are still a significant number of patients who complain of moderate and intense pain in the immediate perioperative period, altering the short-term prognosis of the patients.

![Figure 5. Distribution of VAS static pain score](image-url)
We found that there was a strong correlation between surgery classification according with the anticipated level of pain and static and dynamic VAS score.

In the first postoperative day, 56% of patients from the study had moderate pain at rest and 29% blamed a severe pain. These values decreased gradually so that on day 3 postoperative pain of moderate intensity was present in 37% of subjects, and 15% present severe pain.

The younger patients and women had a lower pain threshold, and a higher VAS score both at rest and cough effort.

Pain induced by diagnostic or therapeutic medical gestures, is rarely taken into account and studies on its incidence is extremely low. In our study, invasive maneuvers performed on the patient have resulted in medium to intense pain, in 48.7% of cases.

8. RESEARCH ON THE IMPORTANCE OF POSTOPERATIVE ANALGESIA IN DAY CASE SURGERY

The study examines the impact of postoperative pain in a group of 44 patients undergoing day case surgery, under general anesthesia, for tonsillectomy.

Figure 11. Average VAS static score according to the administered analgesic medication

In our study, 66.37% of patients had a VAS score > 40, 2 hours after surgery, regardless of the analgesic medication used. The time to first oral intake was shorter and
the general condition of the patients was considerable better for the group with lower VAS score.

There were no significant differences in VAS scores between patients receiving diclofenac, respectively acetaminophen. The patients with parecoxib had a lower average VAS score compared with the group of patients with diclofenac and acetaminophen. This difference was significant in the first 20 hours, after this there were no significant differences in VAS score regarding the three groups.

9. PREEMPTIVE EPIDURAL ADMINISTRATION OF ROPIVACAIN REDUCES THE POSTOPERATIVE PAIN AND DECREASES THE ANALGESIC REQUIREMENTS

We performed a prospective, randomized, study on 46 women scheduled for major abdominal tumour surgery to test the hypothesis that additional preoperative epidural infusion of ropivacaine can reduce the postoperative pain perception and requirement of analgesics in comparison with only systemic intraoperative analgesia.

Visual analogue scale (VAS) pain scores, evaluated at rest and during coughing, the total administered dose of morphine were evaluated at admission to the ICU and then at 2, 4, 6, 12, 24 and 48 hr after surgery.

![Figure 17. VAS values for pain assessed by patients at rest](image-url)
The results of the present study showed that blocking or attenuating noxious inputs before incision, (preemptive analgesia) with epidural ropivacaine, reduced the intraoperative requirements of iv fentanyl and postoperative morphine consumption, as a rescue analgesic. Although the magnitude of this effect was modest, pre-surgical administration of epidural ropivacaine reduced pain on movement, in the early postoperative period after major abdominal surgery.

10. THE STUDY OF EFFICIENCY OF MULTIMODAL ANALGESIA BY LEVOBUPIVACAINE INFILTRATION OF SKIN INCISION

In the group with multimodal analgesia, VAS scores were lower both at rest and at mobilization during the first 24 hours. At 4 hours postoperatively the VAS static score was 35±10.5 while the VAS dynamic score was 39 ± 12 compared with control group B, which at 4 hours postoperatively, have shown values of 50 ± 15.5 at rest and 65 ± 10.5 at mobilization. Significant reduction in pain score occurred postoperatively in both groups after 24 hours.

![Figure 20. Static VAS evolution in the two groups](image-url)
11. CONCLUSIONS

Despite the worldwide increasing interest for a correct management of pain, acute postoperative pain continues to be present in a high percentage in the ICU.

There was a strong correlation between surgery classification according of the anticipated level of pain and static and dynamic VAS score

The younger patients and women had a lower pain threshold, and a higher VAS score both at rest and cough effort.

Our research showed that despite the analgesic treatment during the first postoperative day, 56% of patients experience moderate pain at rest, and 29% have severe pain.

Of the three NSAIDs (paracetamol, diclofenac and parecoxib) used to treat post-tonsillectomy pain, parecoxib, a selective COX2 inhibitor, had the best analgesic effect.

Preemptive analgesia with epidural ropivacaine, reduced the intraoperative requirements of iv fentanyl and postoperative morphine consumption, as a rescue analgesic.

Postoperative evolution of patients with multimodal analgesia (NSAIDs and edge wound infiltration with local anesthetic) is obviously better than patients receiving only iv analgesics, leading to reduced postoperative complications.
PERSONAL INFORMATION

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Articles published in national specialized journals:


**Papers published in international conferences**

G.D. Vârzu, E. Belu, V. Belu, F. Popescu, A. Gusti, S. Gusti The prehospital rapid sequence intubation on outcome of mild brain injured patients, FENS Forum 2008