

**UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA  
DOCTORAL SCHOOL**

**PhD THESIS**

**STUDY CONCERNING THE POSTOPERATIVE PAIN  
THERAPY IN THE MAJOR ABDOMINAL SURGERY**

***ABSTRACT***

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**2016**

*Key words: patients undergoing abdominal surgery; postoperative pain; intravenous analgesia; thoracic epidural analgesia; hemodynamic, respiratory parameters, active mobilisation, return of bowel function; length of hospital stay.*

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## 1. INTRODUCTION

Starting from the principle according to which the therapy of pain is considered by the World Health Organization the 6<sup>th</sup> fundamental human right, this thesis is a study focused on the evaluation of the acute therapy of postoperative pain on patients undergoing major abdominal surgery, with a view to the postoperative recovery, the incidence and severity of side effects given by these, but also the efficiency and complications of epidural analgesia as compared to the intravenous analgesia.

## 2. GENERAL PART

Perioperative pain is strongly triggering the stress reaction, it activates the autonomous system and it is considered to be an indirect cause of the adverse effects on the different systems and organs.

The general part of the thesis has 3 chapters:

1. *Pain* (concept of pain, somatic and visceral sensitivity – anatomic and physiological landmarks).

2. *Mediators involved in transmitting painful stimuli*: nitric oxide; purines; choline; adrenaline and noradrenaline; dopamine; serotonin; exciting and inhibiting aminoacids (gamma-aminobutyric acid, glycine); eicosanoids; platelet activating factor; vanilloid receptors; tachykinins; tissular kinins; cytokines; cholecystokinin.

3. *Data regarding the postoperative analgesia: pharmacological methods* (opioids, nonsteroidal anti-inflammatory drugs, anticonvulsants, tricyclic antidepressants, alfa 2 agonists, N-Methyl-D-Aspartate receptor antagonists, local anaesthetic agents, new therapies, regional or local techniques); *non-pharmacologic methods*: (psychosocial methods, the transcutaneous electrical nerve stimulation, acupuncture, physical rehabilitation, cold, heat).

## 3. SPECIAL PART

***Purpose of the study***: the improvement of the management of acute postoperative pain with patients undergoing major abdominal surgery, in order to obtain the best possible comfort for the patient, with the purpose of a rapid and efficient post intervention recovery, as well as to avoid the apparition of the usual complications for this type of surgical intervention.

***Goals of the study***: the evaluation of the acute postoperative pain in the major abdominal surgery (through visual, numerical, illustrative, multidimensional methods) with the patients hospitalized in the department of Anesthesiology and Intensive Care in the Colentina Clinical Hospital, Bucharest, for a period of 3 years (2011-2013) depending on a series of personal or pathological characteristics, but also in terms of postoperative recovery, of the incidence and seriousness of the side effects induced by analgesia; the monitoring of the hemodynamic and respiratory parameters at different moments after surgery; the evaluation of the need for analgesics; the monitoring of the patient's postoperative evolution, the length of hospital stay;

comparative analysis of the thoracic epidural analgesia and the intravenous analgesia in case of patients undergoing major abdominal surgery under general optimal anaesthesia.

***Material and method of work:***

*The studied lot* comprised 113 patients undergoing major elective abdominal surgery with laparotomy, mainly women (52,2%), the average age being 63,79 years old. Half of the patients in the lot had up to 64 years old, being therefore persons of active age. Most of the patients in the study belonged to the age groups 70-79 years (33,9%), 60-69 (28,8%) and 50-59 years (23,7%), most of men having smaller ages 50-59 (31,5%) and 60-69 years old (27,8%). Most of the patients suffer from comorbidities, most frequently cardiovascular pathology (54%). They showed a form of the neoplastic disease 94,7%, most of cases affecting the gastrointestinal tract and three quarters from the patients (74,3%) were situated in the category of patients with high anaesthetic risk (classes IV and III ASA).

*Methods of study:* patients were divided into two groups: with intravenous analgesia 48,7% and with thoracic epidural analgesia 51,3%. It was of interest: the postoperative care, methods of assessing the quality of postoperative analgesia; the evaluation of hemodynamic and respiratory parameters in different moments after the surgery; the evaluation of the need of analgesic substances used standardly and additionally; the monitoring of the patient's postoperative evolution.

***Results:***

*Results regarding the evaluation of pre and postoperative pain:* preoperatively 95,6% of patients did not feel pain, and postoperatively only 59,3%. Most of patients felt the pain as moderate pain (31%) or slight pain (7,1%), nevertheless 1,8% moderate-severe pain, the situation getting better within 6 to 12 hours and after the first day only a quarter of the subjects would still feel pain, but none of them assessed it as being moderate-severe or severe. Most of patients accusing pain of different intensity were the subjects aged under 65.

*The results regarding the evaluation of the hemodynamic and respiratory parameters* showed that 35,4% of the lot had preoperative high blood pressure, 0,9% low blood pressure, 13,3% bradycardia and 1,8% tachycardia and immediately after the surgery 42,5% had high blood pressure 3,5% low blood pressure, 4,4% bradycardia, 2,7% tachycardia, the situation ameliorating gradually with small fluctuations, so that at 48 hours the share of hypertensives becomes more decreased than that recorded before surgery (28,4%), 3,5% low blood pressure, 8% had bradycardia and no patient tachycardia. After surgery, upon awakening, 21,2% had tachypnea, diminishing within 48 hours to 8%. Between the pain felt postoperatively and the increased values of the systolic arterial pressure at the same moment in time, a correlation was found, that is significant from the statistical point of view (Spearman coefficient 0,404), as well as between the diastolic arterial pressure, the cardiac frequency, the respiratory frequency and the pain score – smaller intensity correlations that are significant from the statistical point of view.

*Results regarding the administered analgesia:* 53,6% of patients needed additional analgesics, most frequently being used the Morphine in bolus (19,6%) and Acetaminophen

(17,8%). 68,9% of patients did not show side effects, the remaining third of patients (31,1%) showed symptoms such as: nausea 8%, sedation 8%, arterial hypotension 5,3%, delirium 4,4%, vomiting or dizziness, each 2,7%. From the point of view of postoperative complications (15%) the most frequent (10,8%) were the surgical complications.

*Results regarding the evaluation of postoperative recovery:* only 3,6% of patients needed ventilation support. The active mobilization was accomplished in average within 2,4 days. The return of bowel function was after 3,12 days. Length of hospitalization was 10,51 days, most of them being hospitalized between 8-14 days (73,4% from the total of the lot), most of women (38,1%) were hospitalized between 8-14 days and among the men (36,3%). Most patients from all age groups were hospitalized between 8 and 14 days: 50-59 years (22,1%), 60-69 and 70-79 years (each 21,2%). Especially men were hospitalized over 3 weeks (3,5% as to 0,9% women) and patients between 70-79 years (1,8%) and one patient from the groups 50-59 years old, 60-69 years old and aged over 80. Side effects had those with a hospital duration of up to 2 weeks. The patients experiencing surgical postoperative complications had the longest durations of hospitalization (over 21 days). From the patients with a hospitalization duration over 2 weeks, most of them were in the anaesthesia risk class ASA III (9,7% of the lot).

*Results regarding the comparative analysis of the epidural and intravenous analgesia:* the epidural anaesthesia was administered to both sexes in equal percentages (25,7% of lot). The intravenous analgesia was administered to 26,5% of women and 22,1% men in the lot. The epidural analgesia was administered in the lot with a bigger frequency than the standard intravenous one in the age groups 60-69 years old (15,9% from the total of the patients included in this age group, as to 12,4% of patients with intravenous analgesia) and in the group aged 50-59 (14,2% as to 13,3% with intravenous analgesia). From the point of view of the ASA risk, those from class III received epidural analgesia in percentage of 34,5% as to 29,2% with intravenous analgesia. Studying the hemodynamic and respiratory postoperative parameters in the two types of analgesia, it came out that regardless of the type of analgesia, most of patients (54% of lot) had normal blood pressure; 22,1% of the patients with epidural analgesia and 20,4% with intravenous analgesia had arterial hypertension upon awakening. Following the progress in time, the situation of the arterial high blood pressure in the two types of analgesia is slightly fluctuating and within 48 hours after surgery it is present in 15% of those with epidural analgesia and in 13,3% patients with intravenous analgesia. Tachycardia is present in a reduced percentage 1,8% in the epidural analgesia and 0,9% in the intravenous analgesia immediately after awakening, the situation becoming normal within 36 hours since both types of analgesias. In what concerns the respiratory frequency, in 78,8% of patients it was normal immediately upon awakening and they showed tachypnea 21,2% (of which 8% with epidural analgesia and 13,3% with intravenous analgesia). The biggest difference was seen at 48 hours in the patients with intravenous analgesia, when it was registered tachypnea 7 times higher than in the patients with epidural analgesia (in these, the percentage was very low-0,9%). Assessing the postoperative pain in the two types of analgesia, we have seen that upon awakening, the pain is felt in 23% of the lot with epidural analgesia and in 17,7% of those with intravenous analgesia. The maximum

pain was at 30 minutes postoperatively in 39,8% both in those with epidural analgesia as well as in those with intravenous analgesia. After 6 hours the pain begins to drop, in both cases of analgesia, thus, at 48 hours it is present in 6,2% in those with epidural analgesia and in 18,6% of those with intravenous analgesia. The additional analgesia was administered to patients that had a scoring assessed on the visual analogue scale of at least 4. Thus, 53,5% of patients needed their medication to be supplemented with postoperative painkillers, for the most of them, 19,6% of the lot needed Morphine and 17,8% Acetaminophen. In patients with epidural analgesia the supplementing was made with Ketoprofen (30,1%), Parecoxib (6%) or Acetaminophen (2,4%), while for those with intravenous analgesia it was used Morphine (29,5%), Acetaminophen (25,3%) and Nefopam Hydrochloride (6,6%). The supplementing with opioids (Morphine) 16,4% was performed in patients with analgesia exclusively intravenous, and with non-opioid analgesic substances (Acetaminophen, Nefopam Hydrochloride, Ketoprofen or Parecoxib) especially in those with epidural analgesia (27,6% of lot, the double as compared to those with intravenous analgesia with 14,5%). The need to supplement the analgesia depending on the intensity of pain felt in different moments after surgery (since waking up to 6 hours) is confirmed by the existence of direct, positive correlations between the scorings of pain and the administration of Morphine and Acetaminophen. Men needed the most the supplementing of analgesia as compared to women (31% as to 23%), the masculine sex representing “a risk factor” that needs the supplementing of analgesia (confirmed statistically). Patients aged under 65 needed in higher extend the supplementing of analgesia, as compared to those aged over 65 (29,2% as to 23,9%). Depending on the ASA risk, the patients having ASA III and IV risk were mostly supplemented Morphine (13,3% of lot) and Acetaminophen (11,5%). As to the induced side effects, the share of those who showed side effects is slightly higher in those with epidural analgesia as to those with intravenous analgesia (43,4% as to 30,1%), the intravenous analgesia being likely to represent a “risk” for the more frequent association with side effects. The postoperative complications were in 11 patients with epidural analgesia as compared to 6 patients with intravenous analgesia. In what concerns the postoperative recovery depending on the type of analgesia practiced, the active movement is produced in the first 3 days for the most part of the patients with both types of analgesia; from the data analysis it resulted that the active movement was more precocious in patients that suffered epidural analgesia as compared to those with intravenous analgesia. The average time of first flatus was 3,12 days (mostly patients with epidural analgesia 41,6% as to the intravenous analgesia in 29,2% of patients), demonstrated statistically that the type of analgesia may influence significantly the time to first flatus. The time to first stool was in average 4,8 days. The length of hospitalization was between 8 and 14 days in 74,3% of patients; the most reduced duration, of up to 7 days was in patients with epidural analgesia, 9,7% of the lot, as to 4,4% of patients with intravenous analgesia.

#### **4. DISCUSSIONS**

The results of this study are represented by the fact that the epidural analgesia is more efficient in the control of postoperative pain, as it is showed in all quoted studies and it is

associated with a more decreased rate of side effects related to opioids. In relation to the postoperative recovery, it was not acknowledged a significant different from the statistical point of view, between the epidural analgesia and that made with morphine, probably also because of a lot of patients much too small in order to be able to study the impact on the hospitalization length.

## 5. CONCLUSIONS

1. This research paper studied a lot of 113 patients undergoing certain major elective abdominal surgeries, with laparotomy, mainly of female sex (52,2%), aged between 30 and 80, the most numerous being in the age group 70-79 years (29,2%) and 60-69 years (28,3%), the average age being 63,79 years. Most of women (33,9%) are in the age group 70-79, and the most numerous men are aged 50-59 years old (31,5%). The research was performed on a period of 3 years (2011-2013), taking into consideration all cases hospitalized in the department of Anesthesiology and Intensive Care, Colentina Clinical Hospital, Bucharest.

2. Almost all patients (94,7%) showed a form of the neoplastic disease (most cases of neoplasias are located in the colon area). From the point of view of the anaesthetic risk, three quarters of patients (74,3%) were situated in the category of patients with high anaesthetic risk (ASA III and IV), in both categories the women being predominant (51,4% and 58,3%) from the age group 60-69 years and 70-79 years old.

3. Immediately after surgery 59,3% accused no pain, the rest assessed the pain as being moderate (31%) or slight (7,1%), the situation being ameliorated in the first half of hour. Most of patients that accused pain were recorded in 30 minutes postoperatively (79,6% from the lot), most of them (45,1%) aged under 65. The cases of severe and moderately-severe pain appear in the first part of the monitoring time frame, until the moment of 12 hours after surgery. The difference between the two age categories in what concerns the perception of pain is significant statistically, the age being likely to represent a "factor" to influence the pain felt after surgery.

4. Has been noted a correlation that is statistically significant between the pain scores and the altered values of some physiological parameters such as the systolic or diastolic arterial pressure, the cardiac and respiratory frequency.

5. The analysis of the hemodynamic parameters in the researched lot pre and postoperatively showed that a third from the total (36,3%) was hypertensive, upon the awakening the percentage raises to 42,5%, later on the percentage of the hypertensive persons being decreased gradually, most drastically in 6 and 12 hours, after 48 hours the percentage becomes more decreased than the one registered preoperatively. There were not remarked alterations in the electric activity of the heart and neither in the activity of the cardiac enzymes.

6. Most patients (51,3%) were administered the standard thoracic epidural analgesia, the rest receiving standard intravenous analgesia (48,7%). The cases with high blood pressure (a fifth) are predominant among those with epidural analgesia, as well as the low blood pressure. The small number of ill people affected by hypoxemia, mainly amongst those with intravenous

analgesia. In most of patients, the respiratory frequency was normal; a quarter of the patients showed tachypnea, especially for those with intravenous analgesia.

7. The pain is perceived postoperatively by 6,2-39,8% from the patients, depending on the moment the assessment was made, with the highest share, in the first 6 hours after surgery, in favour of the moderate pain and in favour of the intravenous analgesia (except for the awakening moment and at 15 minutes).

8. Has been noted a statistically significant correlation between the scores of pain and the additional administration of analgesic substances, the patients with peridural analgesia needing more rarely the supplementing, as compared to those who received intravenous analgesia.

9. Analysing the need of administering the additional analgesia, I have remarked (confirmed statistically) that the masculine sex can represent a “risk factor”, being thus necessary the supplementing of analgesia (31% as to 23% in women). At the same time, patients aged under 65 needed a higher percentage of additional analgesia, as compared with those aged over 65 (29,2% as to 23,9%).

10. Patients from the epidural analgesia lot showed less side effects (43% as to 30%) comparatively with the intravenous analgesia. The difference between the two categories is significant statistically, the intravenous analgesia being likely to represent a “risk factor” for the more frequent association with side effects of analgesic substances. The low blood pressure appeared only in the case of epidural analgesia and the nausea and vomiting appeared more frequently in the intravenous analgesia.

11. In this study only 15% of patients had postoperative complications and these of surgical type (10,8%), the rest of them due to the analgesic technique, these being attributed integrally to the group with thoracic epidural.

12. Most part of the lot is mobilized in the first 3 days, the average of the lot being 2,41 days, as to 2,49 in the sub-lot with intravenous analgesia 2,33 in the epidural analgesia, late mobilization (after 4 days), predominantly in patients with intravenous analgesia.

13. For most of patients time of first flatus was within the first 4 days, the average duration in the lot being of 3,12 days, as to 2,93 the average in the sub-lot with epidural analgesia and 3,33 in the sub-lot with intravenous analgesia, with double late recovery of the bowel function in those with intravenous analgesia, therefore a statistically significant difference, which indicates the fact that the type of analgesia administered may influence significantly the recovery of the bowel function, an intravenous analgesia representing a “factor” which could lead to a delayed gas passage.

14. For most of patients time of first stool was within the first 5 days, the average duration being 4,8 days, as compared with an average of 4,66 for patients with thoracic epidural and 5,07 for those with intravenous analgesia, the tardive recovery of defecation, after the 6<sup>th</sup> day, appears especially in the sub-lot with intravenous analgesia.

15. Most of patients (74%) had a hospitalization comprised between 8 and 14 days, the average duration being 10,51 days, as compared to an average of 10,4 days in the sub-lot with epidural

analgesia and 10,64 days in the sub-lot with intravenous analgesia, the type of analgesia not influencing the length of hospitalization.

***Final conclusion. Originality of the study.***

***This wide, complex research concerning the efficacy of postoperative analgesia with the purpose of rapid recovery, with no complications in the risky patients, is less mentioned in the literature.***

***The compared study regarding the thoracic epidural analgesia and the intravenous analgesia highlighted the superiority of epidural analgesia due to the superior quality of analgesia, faster active movement and faster bowel function recovery.***

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