

## Dexmedetomidine Might Reduce the Incidence of Chronic Post-operative Pain after Major Abdominal Surgery

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### Abstract

**Aim:** To evaluate influence of dexmedetomidine on incidence of chronic postoperative pain and neuropathic pain.

**Background:** Chronic postoperative pain (CPSP), pain that cannot be explained by other causes and that persist more than 2 months after surgery, occurs in 10-50% of patients after the major abdominal surgery. It is a medical problem with huge economic implications. Intraoperative infusion of dexmedetomidine (DEX), a selective alpha2 adrenoreceptor agonist and presence of epidural analgesia may affect the incidence of CPSP.

**Method:** Adult surgical patients from the Clinical department of abdominal surgery UMC Ljubljana that were planned to undergo one of the following procedures: stomach surgery, pancreas surgery or large intestinal resections, were included in this prospective study. All patients had epidural analgesia and intraoperative DEX infusion. Three months after the procedure, structured questionnaire was send to patients. The intensity and quality of pain were examined. DN4 (Douleur Neuropathique 4) and painDetect questionnaires were used.

**Results:** We have received 42 (50%) properly filled DN4 questionnaires and 45 (53%) pain-detect questionnaires. The incidence of neuropathic pain in our study was 7.1% (3 patients have met criteria for neuropathic pain according to DN4).

**Conclusion:** Our prospective study might suggest a favorable role of intraoperative dexmedetomidine infusion on post-operative incidence of chronic postoperative pain

**Keywords:** Dexmedetomidine; Neuropathic pain; Abdominal surgery

### Introduction

There is a growing number of studies exploring the incidence of chronic postoperative pain (CPSP), pain that cannot be explained by other causes and that persist more than 2 months after surgery [1]. Neuropathic characteristics are often present. Reported incidence in abdominal surgery is 10-50% [2,3]. It is a medical problem with huge economic implications. In one-third of the patients consulting pain clinics, pain is consecutive to surgery [4]. For abdominal surgery, a randomized controlled study with 85 patients showed a beneficial effect on acute postoperative and long-term pain up to 12 months after surgery in patients who received perioperative epidural analgesia combined with ketamine infusion [5]. Other reports have also confirmed benefits of epidural analgesia alone [6].

Dexmedetomidine (DEX) is selective alpha2 adrenoreceptor agonist. It has a short terminal half-life (2 hr.), produces antinociception, e.g. by reducing hyperalgesia, inhibits the activation of microglia cells and signal regulated kinase in spinal dorsal horn after nerve injury, decreases the demand of intraoperative anesthetics and reduces the perioperative catecholamine release [7]. Peripheral administration of dexmedetomidine reduces mechanical and heat hyperalgesia and mitigates postoperative pain [8]. The growing number of evidence suggest beneficial effect of DEX and epidural analgesia on CPSP after major abdominal surgery. The aim of our study was to evaluate influence of DEX on incidence of CPSP and neuropathic pain.

### Materials and Methods

Adult patients, ASA (American Society of Anesthesiologists) Class 2-3 surgical patients from the Clinical department of abdominal surgery UMC Ljubljana that were planned to undergo one of the following procedures: stomach surgery, pancreas surgery or large intestinal resections, were included.

All patients were visited by a member of our team a day prior to surgery to seek an informed consent and to answer any questions. Only patients scheduled for elective procedure with suspected carcinoma were included. Patients with contraindications for epidural analgesia and patients with planned postoperative stay in ICU were excluded. Patients were admitted to preoperative preparation area immediate before the surgery. After monitoring and iv-line placement, dexmedetomidine infusion was started (0.5 mcg/kg/hour). Continuous infusion ended after skin suture at the end of the procedure.

Thoracic epidural catheter insertion in left lateral position was performed before the beginning of the procedure. Intraoperative analgesia was achieved with levobupivacaine epidurally and supplementation of sufentanyl. PCEA was used for postoperative analgesia. Epidural block was considered efficient if no supplemental analgesia was needed during operation. Patients with inefficient block were excluded from the study. Three months after the procedure, structured questionnaire was send to patients. The intensity and quality of pain were examined. DN4 (Douleur Neuropathique 4) [9] and painDetect [10] questionnaires were used. Answers were collected, and statistical analysis was made using the IBM SPSS software 22 (New York, USA). P value of 0.05 was considered statistically significant. The study was approved by National Medical Ethics Committee of Slovenia and registered in ClinicalTrials.gov (NCT02293473).

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## Results

Questionnaires were sent to 84 patients between years 2015-2017. We have received 42 (50%) properly filled DN4 questionnaires and 45 (53%) painDetect questionnaires. The results are shown in Tables 1, 2 and 3. 42 patients with both questionnaires properly filled were analyzed. Average age of included patients was 65 ( $\pm 12$ ) years; average weight was 64  $\pm$  10 kg. 17 patients of ASA 2 status and 25 ASA 3 patients were included. 20 (48%) patients were male, 22 were female. 2 out of 84 patients underwent pancreas surgery; however, they were not among the returned questionnaires. The results of other subgroups are seen in Table 4. The incidence of neuropathic pain in our study was 7.1% (3 patients have met criteria for neuropathic pain according to DN4).

## Discussion

Our study shows relatively low incidence of CPSP among our patients (7.1% incidence of neuropathic pain and no chronic pain estimated more than 7 on Numeric rating scale), comparing the data from the literature [1-3]. Pain behavior pattern in painDetect [10] shows majority of patients in patterns of pain [first and second pattern in the Table 3] that are less likely of neuropathic origin. Methods in studies differ and are not directly comparable, but they usually they report higher incidence of CPSP, 17% in study of Joris et al. [2] for laparoscopic colorectal surgery and similar incidence for laparotomy. Although epidural analgesia significantly decreases incidence of CPSP [6], the reported incidence (17.6%) is still higher than in our study [6]. This might suggest a favorable role of DEX infusion [8]. There is no statistically significant difference in CPSP in both subgroups, stomach and intestine surgery. The group is too small to analyze the influence of comorbidities, that may significantly affect CPSP [3,10]. 1 out of 5 (20%) insulin dependent diabetics developed CPSP.

## Study limitations

We have achieved only moderate response (53%) from patients. It is not possible to exclude the possibility that only the patients with favorable surgical outcome have sent their answers. This gives us falsely better numbers than they are. We did not analyze the psychological factors, such as depression that play an important role in CPSP.

## Conclusion

The aim of our study was to find out the incidence of CPSP among our patients. There was no control group without DEX. Our prospective study might suggest a favorable role of intraoperative dexmedetomidine infusion on post-operative incidence of chronic postoperative pain.

Sensory descriptors or sensory dysfunction	Number of patients with positive answer (%)
Burning pain	3 (7.1)
Painful cold	2 (4.8)
Electric shocks	1 (2.4)
Pins and needles	11 (26.2)
Tingling	4 (9.5)
Numbness	2 (4.8)
Itching	4 (9.5)
Touch hypoaesthesia	0 (0)
Prick hypoaesthesia	0 (0)
Pain increased by brushing	0 (0)
4 or more positive at the same patient (meets the criteria for neuropathic pain)	3 (7.1)

**Table 1:** Frequency of sensory descriptors or sensory dysfunction, answers to DN4 questionnaire.

Variables	Mean (std. deviation), minimum - maximum
Pain level in given moment	1.2 ( $\pm 1.4$ ), 0 - 5
Maximum pain in last 4 weeks	5.3 ( $\pm 2.7$ ), 1 - 10
Average pain in last 4 weeks	2.2 ( $\pm 1.6$ ), 0 - 7

**Table 2:** Analysis of pain-detect questionnaires (numerical rating scale 0-10).

Variables	Frequency (%)
Persistent pain with slight fluctuations	12 (26.7)
Persistent pain with pain attacks	19 (42.2)
Pain attacks without pain between them	6 (13.3)
Pain attacks with pain between them	4 (8.9)
Missing answer	4 (8.9)

**Table 3:** Pain behaviour pattern in pain-detect questionnaire.

Type of surgery	Stomach surgery	Intestinal surgery	inference
No. of patients	16	26	Total 42
Duration of the procedure	123 min (IQR 35 min)	130 min (IQR 40 min)	p=0.122 (Mann – Whitney U test)
No. of patients with admission to intensive care unit	1	0	p=0.381 (Chi-Square test)
Readmission of patients to high dependency unit	1	5	p=0.380 (Chi-Square test)
No. of patients with insulin dependent diabetes (No. of them with neuropathic pain)	3 (0)	2 (1)	p=0.352 (Chi-Square test)
Average length of stay in hospital	9 (IQR 3)	9 (IQR 4.5)	p= 0.651(Mann – Whitney U test)
No. of patients who met criteria for neuropathic pain	2	1	p=0.547 (Chi-Square test)

**Table 4:** Results of sub-groups included in the study

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