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A comparison of the different regional anesthesia methods efficacy in chronic pain syndrom prevention in lung cancer surgery

Submission date
29/01/2018

Recruitment status
No longer recruiting

Registration date
01/02/2018

Overall study status
Completed

Last Edited
17/03/2023

Condition category
Respiratory

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Despite the development of surgery technics, thoracotomy (incision of the thoracic wall) still has a place for lung cancer surgery. In patients undergoing thoracotomy the postoperative period can be the source of acute postthoracotomy pain. From 38% to 63% of patients report acute pain, which the intensity ranges from moderate to severe. The development of pain results in an impaired breathing activity. This can leeds to of lung infection disturbance, loss of appetite and a significant decline in their quality of life. Chronic post-thoracotomy pain syndrome is one of the most often side effects in lung surgery. After thoracotomy, its incidence ranges from 30% to 40%. The chronic postoperative pain is defined as pain that develops after surgical intervention and lasts for at least 2 months (International Association for the Study of Pain). In our study, we aimed to assess the influence of the three different methods of anesthesia on the incidence of the CPTPS.
300 patients, undergoing lung cancer surgery using thoracotomy were randomized into three groups: 1) 100 patients - thoracic epidural anesthesia ; 2) 100 patients - paravertebral nerve block ; 3) 100 patients – intercostal nerve block . It means that they recived differed methods of anesthesia.
Postoperatively, patients were requested to evaluate their pain intensity on the spetial scale. It was assessed at rest and at moving in 7 days, 1 and 6 months after surgery.
We compared the pain intensity between different groups and between the time points. We aimed to find besser methods of anesthesia in chronic pain prevention.

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
№ 12-09

Study information

Scientific Title
Influence of regional anesthesia component on the rate of chronic post-thoractomy pain syndrome in lung cancer patients

Study objectives
It is expected that a difference at the chronic pain syndrome 13.8% between paravertebral nerve block and thoracic epidural anesthesia and minimally 20% reduction as compared with intercostal nerve block.

Ethics approval required
Old ethics approval format

Ethics approval(s)
IRB of the P.A. Herzen Moscow Cancer Research Institute, 10/01/2012, ref: № 12-09

Study design
300 patients, undergoing lung cancer resection using thoracotomy. Participants are randomised into three groups: 1) 100 patients - thoracic epidural anesthesia ; 2) 100 patients - paravertebral nerve block ; 3) 100 patients – intercostal nerve block .

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)

Prevention

Participant information sheet
See additional files (in Russian)

Health condition(s) or problem(s) studied
Chronic post-thoracotomy pain syndrome (CPTPS) is one of the most often side effects in lung surgery. After thoracotomy, its incidence ranges from 30% to 40%. The CPTPS is defined as pain that develops after surgical intervention and lasts for at least 2 months (International Association for the Study of Pain). The mechanism of the CPTPS is a long-lasting non-curable acute surgical pain associated with surgical trauma and inflammation of chest wall, lung and pleural parenchyma. For this reason, the APTPS should be effectively prevented and treated as soon as possible. In addition, the presence of a neuropathic component due to injury or irritation of the intercostal nerves is reported, as a mechanism of the pain chronicization. The emergence of a neuropathic pain component is critical for thoracotomy and thoracoscopy due to the features of the chest wall innervation and the surgical techniques.

Interventions
All consecutive patients scheduled for thoracotomy are randomly assigned to into three groups: 1) thoracic epidural anesthesia (TEA) ; 2) paravertebral nerve block (PVB) 3) intercostal nerve block (INB) using Research Randomizer (http://www.graphpad.com).

In the TEA group, an epidural catheter is placed at T4-T6 interspace before induction. Then the intra-epidural infusion of ropivacaine 0.3%, fentanyl 4 μg/mL and epinephrine 2 μg/mL is started at 5-15 mL/h. Postoperatively, this group received an anesthetic solution containing ropivacaine 0.3%, fentanyl 4 μg/mL and epinephrine 2 μg/mL for 2 days. After day 2, ropivacaine 0.2% was infused alone until the 5th postoperative day.

In the PNB group, paravertebral catheter was placed using ultrasound at the T5-T6 level. Before the induction of general anesthesia, the patients received a bolus of lidocaine 2% - 10 mL and the same anesthetic solution as the TEA group in the volume of 20 ml. At the end of surgery, a second bolus dose (20 ml) of the anesthetic solution was administered. Postoperatively the patients received the anesthetic solution (as in TEA group) with an infusion rate at 8-12 mL/h during the first 2 days, and then this solution was changed to ropivacaine 0.2% and the infusion was prolonged until the 5th postoperative day.

In the INB group, an intercostal nerve block was provided by the surgical team after the lung or lobe resection. A solution of ethanol 96% - 30 mL and novocain 0.5% - 30 mL was mixed and injected into the intercostal space subpleuraly paravertebraly just below the intercostal nerve at three levels (20 mL of solution at each level) to provide the intercostal block at the level of thoracotomy, above and below the incision as it was described in the literature [40,41]. Postoperatively, additional injections of a local anesthetic were administered transdermally in the patients with acute pain syndrome defined by a visual analog score (VAS) above 50 mm. The patients received 0.5% solution of novocaine – 20 mL at the same levels. The needle was placed at an angle of approximately 20° cephalad to the skin in the paravertebral line. The needle was kept away from the lower border of the rib, as the skin returned to its initial position. Then the needle was placed 3 mm below the inferior margin of the rib, with the goal of placing the tip in the space containing the neurovascular bundle (i.e., between the internal and innermost intercostal muscles).

The patients in all groups received oral pregabalin 75 mg twice a day before surgery and once on the day of surgery, 2 hours before anesthesia induction. After surgery, pregabalin (75 mg twice daily) was continued until hospital discharge. Patients received lornoxicam 8 mg preoperatively and twice a day after surgery. Nefopam 20 mg was administered intramuscularly 40 minutes before the end of the surgery for hyperalgesia prevention and continued from the onset of initial pain syndrome during for 5 days (20 mg x 2 per day). In the case of persistent pain syndrome, morphine 10 mg was additionally prescribed on the patient request or if VAS was > 50 mm.
General anesthesia was similar in the three groups. Propofol 2 mg/kg, fentanyl 0.002 mg/kg, ketamine 25 mg, and rocuronium 0.6 mg/kg were administered for induction. Ventilation was mechanically controlled and adjusted to maintain end-tidal CO2 at 30–35 mmHg, inspired fraction of O2 at 35%. After endotracheal intubation anesthesia was maintained with sevoflurane (0.8-1 MAC), fentanyl (0.05-0.1 mg IV every 15-30 min, when the SBP increased by more than 15% from the baseline value or was > 140 mmHg). Rocuronium was administered for muscle relaxation, based on TOF response.

Horizontal VAS was used to assess the intensity of pain syndrome. Patients were requested to mark their pain intensity on that scale: 0 = no pain and 100 mm = worst possible pain. Static and dynamic pain components were assessed in 7 days, 1 and 6 months after surgery. Static pain component was measured at rest. Dynamic pain component was accepted as the highest intensity of pain during normal daily activity, deep breathing and maximal coughing. On the 7th day after surgery the intensity of pain was assessed during a consultation in the patient room. On discharge patients received VAS and then were interviewed by telephone 1 and 6 months after surgery. The intensity of pain syndrome 1-30 mm was considered as mild, 31-70 mm – moderate, more 70 mm – severe. The pain syndrome (VAS ≥1 mm) at day 7 and month 1 after surgery was accepted as APTPS, pain syndrome at month 6 – CPTPS.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Frequency and intensity of the CPTPS is measured using the Visual Analogue Scale (0 = no pain and 100 mm = worst possible pain) at 6 months after surgery
2. Effectiveness of TEA, PVB, and INB in CPTPS prevention are measured using the Visual Analogue Scale (0 = no pain and 100 mm = worst possible pain) at 6 months after surgery

Secondary outcome measures
1. Intensity of APTPS and CPTPS between groups are measured using the Visual Analogue Scale (0 = no pain and 100 mm = worst possible pain) at 7 days, 1 and 6 months after surgery.
2. Pain is measured using the Visual Analogue Scale (0 = no pain and 100 mm = worst possible pain) at 7 days, 1 and 6 months after surgery

Overall study start date
17/10/2011

Completion date
28/07/2017

Eligibility

Key inclusion criteria

All consecutive patients scheduled for thoracotomy were screened for study inclusion using the following eligibility criteria: adult patients and ASA physical status from I to III.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
3 clusters, not less than 90 at each claster

Total final enrolment
300

Key exclusion criteria
1. General anesthesia within 7 days before study inclusion
2. Administration of experimental drug within 30 days before surgery
3. Preoperative chronic postoperative pain syndrome
4. Acute unstable angina
5. Acute myocardial infarction documented by laboratory findings in the past 6 weeks
6. Heart rate (HR) < 50 beats per min (bpm)
7. Systolic blood pressure (SBP) < 100 mmHg
8. Heart block
9. Pre-operative vasopressor administration

Date of first enrolment
11/01/2012

Date of final enrolment
22/06/2016

Locations

Countries of recruitment
France

Russian Federation

Study participating centre
P.A. Herzen Moscow Cancer Research Institute
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Study participating centre
Aix Marseille Université
APHM. Hôpital Nord
Service d'Anesthésie et de Réanimation
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Sponsor type
Hospital/treatment centre

Website
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ROR
https://ror.org/04rbazs75

Funder(s)

Funder type
University/education

Funder Name
P.A. Herzen Moscow Cancer Research Institute

Results and Publications

Publication and dissemination plan
Plans to present results at international conferens (ESA 2017), to publish results in russian (https://www.ncbi.nlm.nih.gov/pubmed/28805780), and to publish our results for an international audience in a journal with a large diffusion. Protocol and other documents (in Russian) are available upon request.

Intention to publish date
29/08/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Danil Baskakov Danil_Bask@mail.ru or co investigator Dr. Malanova Anna: malanova_anna@mail.ru.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		31/01/2018	01/04/2019	No	Yes
Results article		20/06/2018	17/03/2023	Yes	No