ISRCTN13000406 https://doi.org/10.1186/ISRCTN13000406

Injection of dexmedetomidine into the paravertebral space (where the nerve for the chest section comes out of the vertebra) protects against lung injury during lung surgery when only one lung is being inflated by a breathing machine

Submission date 15/05/2018	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 21/05/2018	**Overall study status** Completed	
Last Edited 22/02/2019	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
During lung surgery, the entry of air is blocked to the diseased lung so that it is not moving during the operation. The healthy lung is supplied with air using a ventilator (breathing machine). In a small proportion of patients, the non-ventilated lung can become swollen and stop working properly in the days after surgery. The risk of death in these patients is high. This study aims to investigate whether injection of the sedative (consciousness-reducing) drug dexmedetomidine into the paravertebral space (space next to a vertebra where a nerve exits the spinal column) can reduce swelling, inflammation and cell death in the non-ventilated lung.

Who can participate?
Adults aged 18 to 65 years who are having surgery to remove lung cancer.

What does the study involve?
The patients will receive intravenous (by vein) saline (salt solution), intravenous dexmedetomidine, or paravertebral injections of the anaesthetic (sensation-blocking) drug ropivacaine alone or paravertebral ropivacaine in combination with one of three doses of dexmedetomidine. The cancer will be removed as usual and samples of the lung tissue containing the tumour will be tested for signs of swelling, inflammation and cell death.

What are the possible benefits and risks of participating?
There are no known additional risks or benefits to participating. Patients will receive surgery as usual. Ropivacaine and dexmedetomidine are safe and widely-used drugs.

Where is the study run from?
Henan Provincial People's Hospital

When is the study starting and how long is it expected to run for?
July 2016 to March 2017

Who is funding the study?
The Natural Science Foundation of China and Henan Province, the Science and Technology Project of Henan Province and the Medical Science Research Project of Henan Province

Who is the main contact?
Prefessor Jiaqiang Zhang
mazuizhang@163.com

Contact information

Type(s)
Scientific

Contact name
Prof Jiaqiang Zhang

Contact details
No.7 Weiwu Road, Zhengzhou City, Henan ProvinceChina
Zhengzhou
China
450003

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Paravertebral dexmedetomidine as an adjuvant to ropivacaine protects against lung injury in the non-ventilated lung during one-lung ventilation

Study objectives
We hypothesized that paravertebral dexmedetomidine would alleviate lung injury as effectively as intravenous dexmedetomidine.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Henan Provincial People's Hospital ethics committee, 18/09/2017

Study design
Randomized blinded single-centre study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Acute lung injury following selective radical resection for pulmonary carcinoma

Interventions
In total, 120 patients who underwent elective radical resection of pulmonary carcinoma were randomly assigned to one of six groups (n=20): normal saline (C group), ropivacaine (R group), intravenous dexmedetomidine (Div group), 0.5 μg/kg paravertebral dexmedetomidine as an adjuvant to ropivacaine (RD0.5 group), 1.0 μg/kg paravertebral dexmedetomidine as an adjuvant to ropivacaine (RD1.0 group), or 2.0 μg/kg paravertebral dexmedetomidine as an adjuvant to ropivacaine (RD2.0 group). Thoracic paravertebral block (TPVB) was induced under ultrasound guidance (S-Nerve, Fujifilm Sonosite, Inc). TPVB was not administered in the C or Div groups. Patients in the C group received only normal saline as a control; patients in the R group received a total volume of 20 ml 0.5% ropivacaine for the TPVB (cat No. NATM, AstraZeneca, Sweden), with 10 ml injected at each puncture point; patients in the Div group received a total dosage of 0.5 μg/kg intravenous dexmedetomidine (cat No. 20160301, Jiangsu Nhwa Pharmaceutical Co., Ltd, China) over 10 min; and patients in the RD0.5, RD1.0 and RD2.0 groups received ropivacaine (final concentration of 0.5%) mixed with 0.5 μg/kg, 1.0 μg/kg and 2.0 μg/kg dexmedetomidine, respectively, as an adjuvant. Only one anesthesiologist who was blinded to the group allocation was involved in the preoperative management.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)

dexmedetomidine, ropivacaine

Primary outcome measure
Lung injury score.
Method: The histological changes of the fixed lung tissue were evaluated by an independent pathologist who was blinded to the study protocols. The lung tissues were embedded in paraffin wax, sectioned (5 μm), and then stained with hematoxylin and eosin. The severity of lung injury was quantified using the 4-point scoring system, which included pulmonary interstitial edema, alveolar edema, alveolar congestion and neutrophil infiltration. Scoring standards were as follows: 0, no change or very mild changes; 1, mild changes; 2, moderate changes; and 3, severe changes. The average lung injury score from three adjacent slices was evaluated. The summation of four scores was recognized as the final lung injury score.
Time point: Immediately after the tumor tissue was excised

Secondary outcome measures
1. Hemodynamics (heart rate, mean arterial pressure) measured using the ECG monitor and invasive arterial pressure system. Time points: preoperative (Pre) - 15 min after admission to the operating room without any drug treatment, two-lung ventilation (TLV) - immediately before initiation of one-lung ventilation (OLV), OLV1 - 15 min after initiation of OLV, OLV2 - 30 min after initiation of OLV, OLV3 - immediately before the tumor tissue was excised
2. Apoptosis measured using a TUNEL assay employed according to the manufacturer's protocol of an in situ cell death detection kit-POD (cat no. 11684817910; Roche, Basel, Switzerland). Apoptotic cells were indicated by brown-yellow granules in the cytoplasm. The number of apoptotic cells in random fields of view (magnification, x400) was calculated. The apoptosis index (AI; %) was expressed as follows: the number of apoptotic cells/the total number of cells x100. The slides were prepared immediately after tumor excision.
3. Inflammatory cytokines measured by enzyme-linked immunosorbent assay (ELISA). Lung tissues were prepared as 10% tissue homogenates and centrifuged at 3000 rpm at 4°C for 10 min. The supernatant was collected for further analysis. The concentrations of TNF-α and IL-6 in lung tissues were measured according to the manufacturer's instructions using ELISA kits (Nanjing Keygen Biotech Co., Ltd.). Absorbance at 450 nm (OD 450) was determined using a microplate reader. The tissues were prepared immediately after tumor excision.

Overall study start date
01/06/2016

Completion date
01/03/2017

Eligibility

Key inclusion criteria
1. American Society of Anesthesiologists (ASA) physician status I or II
2. Aged 18-65 years
3. Scheduled for selective radical resection of pulmonary carcinoma

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
Six groups of 20 patients

Key exclusion criteria
1. Hypertension
2. Diabetes mellitus
3. Heart diseases
4. Suggestive history of inflammation or coagulation dysfunction

Date of first enrolment
01/07/2016

Date of final enrolment
01/02/2017

Locations

Countries of recruitment
China

Study participating centre
Henan Provincial People's Hospital
China
450003

Sponsor information

Organisation
Henan Provincial People's Hospital

Sponsor details
No.7 Weiwu Road, Zhengzhou City, Henan Province
Zhengzhou
China
450003

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03f72zw41

Funder(s)

Funder type
Not defined

Funder Name
The Natural Science Foundation of China and Henan Province (U1404807)

Funder Name
Science and Technology Project of Henan Province (182102310167)

Funder Name
Medical Science Research Project of Henan Province (201602227)

Results and Publications

Publication and dissemination plan
Submitted to BMC Anesthesiology

Intention to publish date
01/08/2018

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/06/2018		Yes	No