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Epidural hydromorphone vs epidural morphine for the management of pain in old patients with postherpetic neuralgia

Submission date
25/05/2019

Recruitment status
No longer recruiting

Registration date
06/06/2019

Overall study status
Completed

Last Edited
19/07/2023

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
About 20% of patients with Herpes zoster develop postherpetic neuralgia (PHN), with which patients may continue to experience pain for months to years after the resolution of the rash caused by the virus. The incidence of PHN is 4/1000 per year. Advancing age and severity of acute Herpes zoster pain are the strongest risk factors for PHN. The disease usually occurs between 50 and 79 years of age. PHN results in suffering, reduced quality of life, and individual as well as societal healthcare costs.
Current therapies still do not control the refractory pain caused by PHN effectively. Morphine is a hydrophilic opioid that is usually epidurally administered for postoperative analgesia. It can be administered as a continuous epidural infusion at a dose of 0.1 to 0.4 mg/hour for the treatment of neuropathic pain for a long time in China. However, there is no RCT to compare the efficacy and safety of hydromorphone Vs morphine in epidural administrations for PHN.

Who can participate?
Elderly patients (50y ≤ age ≤ 80y), with refractory pain caused by post-herpetic neuralgia.

What does the study involve?
Participants are randomly allocated to two groups. Those in group 1 are given epidural hydromorphone infusion for 2~3days. Those in group 2 are given epidural hydromorphone infusion for 2~3days instead. The pain experienced before and after the treatment is assessed for each patient.

What are the possible benefits and risks of participating?
The participants could have better pain relief. The main possible risks are the side effects of opioids or adverse events associated with epidural catheterization.

Where is the study run from?
Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China.

When is the study starting and how long is it expected to run for?
May 2019 to January 2022

Who is funding the study?
Science and Technology Commission of Shanghai Municipality, China

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
XINHUA2019-01

Study information

Scientific Title
Epidural hydromorphone vs epidural morphine for the management of pain in patients between 60 to 80 years old with postherpetic neuralgia: a randomized, double-blind, parallel-controlled, non-inferiority study

Study objectives
The aim of this study was to test noninferiority of epidural hydromorphone versus epidural morphine for the management of pain in elderly patients with postherpetic neuralgia during and after the treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 28/04/2019, Ethics Committee of Xinhua Hospital (Shanghai Jiao Tong University School of Medicine, 1665 Kongjiang Rd, Shanghai, P.R China, 200092; Tel: +86-21-25076141; xinhuahospitalec@163.com), ref: XHEC-C-2019-015-1

Study design
Single-center randomized double-blind parallel-group controlled two arm non-inferiority trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Postherpetic neuralgia

Interventions
Patient enrollment and allocation:
Eligible patients will be admitted to hospital and included in the study after screening and signing the informed consent, then, they will be 1:1 randomized assigned to receive either epidural hydromorphone infusion (intervention group) or epidural morphine infusion (control group), according to the random table generated by the statistics software.
Treatment procedures:
Before the placement of the epidural catheter, all patients received oral gabapentin 300 mg t.i.d. as basic treatment. A catheter will be placed to the epidural space under the fluoroscopic guidance after percutaneous puncture, the tip of the catheter will be placed at the spinal level corresponding to the peripheral afferent sensory nerves of the personally affected dermatome. Then, the extracutaneous portion of the catheter will be temporarily secured and connected to an external electronic infusion pump, which has a PCA bolus infusion function. A pre-prepared reservoir, containing hydromorphone solution(2mg/100ml NS) or morphine solution (10mg /100ml NS) in the blind state, will be installed in the pump. The initial infusion rate was 1.5 ml /hour and the bolus infusion was 1.5 ml/press/2 hour.
Duration of treatment:
Continuous infusion time is 2~3 days. The overall duration of patient participation from screening to the end of the treatment period study will be approximately 4~5 days. After the infusion, the catheter will be pulled out and the patient will continue to receive treatment according to the Chinese guidelines for neuropathic pain.
Provision of drugs:
All of the aforementioned drugs have been approved in China for the treatment of pain. They will be prescribed by clinicians according to the usual procedures in use and dispensed by the Urban Residents Healthcare Service of Shanghai. The drug reservoir will be prepared before the epidural procedures by a non-blind staff/nurse of Pharmacy Department following GMP, according to the randomized allocation.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

1. Hydromorphone Hydrochloride Injection (manufactured by Yichang Humanwell Pharmaceutical Co., Ltd, Hubei, China) 2. Morphine Hydrochloride Injection (manufactured by Northeast PHARM Co., Ltd, Liaoning, China)

Primary outcome(s)
1. Pain intensity in the first three days measured with VAS, twice a day, at 09:00 and 21:00, after epidural opioid infusion, calculated as the average value of VAS during treatment at 1, 2 and 3 days after drug administration is the main outcome measure.
The time point for pain assessment during the long-term follow-up phase will be the 7th day, 14th day, 21st day, 28th day, 60th day and 90th day after the start of treatment.

Key secondary outcome(s))
1. Daily occurrence of breakthrough pain measured using pain diary kept by participants, daily from baseline to end of study.
2. Quality of Life (QoL) measured using WHOQOL-OLD
3. PCA bolus press number (no. of patient-controlled epidural analgesia button press during the treatment), during the treatment days (the 1st day, 2nd day, 3rd day after the start of the treatment).
4. Assessment of anxious/depressive disorders (scored with GAD-7 and PHQ-9) at baseline, the 1st day, 2nd day, 3rd day, 7th day, 14th day, 21st day, 28th day, 60th day and 90th day after the start of treatment.
5. Safety & Tolerability, including opioid-related side effects and Epidural procedure related complications (adverse drug reactions, adverse events and serious adverse events occurring during the study) measured using patient self-report, reviewing patients' notes, patient interviews, medical records, etc. throughout the study period.

Completion date
30/05/2020

Eligibility

Key inclusion criteria
1. 50 years ≤ age ≤ 80 years, regardless of gender.
2. Active post-herpetic neuralgia with refractory pain more than 30 days after rash onset.
3. Stable anti-neuropathic-pain therapy according to the guidelines of IASP NeuPSIG (> 7 days), still VAS ≥ 50mm.
4. Ability to objectively describe symptoms, actively follow the physician's medication recommendation and cooperate with physicians for diagnosis, treatment and follow-up.
5. Written informed consent to study participation.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex

All

Total final enrolment
80

Key exclusion criteria
1. Contraindications to epidural catheterization or opioids
2. Allergy to medications or devices related to the trail
3. Cognitive deficits compromising the ability to assess pain or pain relief
4. Previous therapy with hydromorphone or morphine
5. Pregnancy or breastfeeding
6. Drug abuse or drug addiction history
7. Severe hepatic and/or renal impairment
8. Epidural anesthesia in last 3 months
9. Participation in other clinical trials that might interfere with the study results

Date of first enrolment
30/05/2019

Date of final enrolment
31/05/2020

Locations

Countries of recruitment
China

Study participating centre
Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine
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Sponsor information

Organisation
Science and Technology Commission of Shanghai Municipality

ROR
https://ror.org/03kt66j61

Funder(s)

Funder type
Government

Funder Name
Science and Technology Commission of Shanghai Municipality

Alternative Name(s)
Shanghai Municipal Science and Technology Commission, Shanghai Science and Technology Committee, , STCSM

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
China

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		06/12/2022	19/07/2023	Yes	No