Randomized clinical trial of the optimization of procedural pain control in ICU patients

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON31005

Source
ToetsingOnline

Brief title
OPCIC

Condition

- Other condition

Synonym
pain relief

Health condition

Patiënten op de ICU, zowel electief als niet electief opgenomen

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W,salaris van de promovendus wordt gedurende 2 jaar medegefinancierd door het pijnkenniscentrum te Rotterdam;voor het overige geldt de eerste geldstroom

Intervention

Keyword: Intensive Care, Morphine, NRS, Pain

Outcome measures

Primary outcome

The percentage of patients with a NRS of >= 4 during intervention (2.5 mg versus

7.5 mg morphine)

Secondary outcome

- The mean NRS during an intervention (2.5 mg versus 7.5 mg morphine)

- The mean NRS during an intervention (2.5 versus 7.5 mg morphine) corrected

for baseline NRS

- The percentage of patients with at least one NRS-score of >= 4 at rest during

ICU stay

- The mean NRS per patient in rest during ICU stay

- The percentage of patients with a NRS of >= 6 during intervention (2.5 mg

versus 7.5 mg morphine)

- Pharmacokinetic parameters of morphine (volumes of distribution and clearance

values)

- Pharmacodynamic parameters of morphine (EC50 etc)

- Covariates for the PK/PD of morphine (body weight, age, renal function

(ureum, creatinin concentrations and creatinin clearance), liver function,

diagnose, Sequential Organ Failure Assessment (SOFA) scores, DNA polymorphisms (μ-opioid receptor, COMT etc) and perioperative endorphins and stress hormones (epinephrine and norepinephrine), level of sedation and/or concentration of sedative (propofol).

- Safety and other measures (nausea, constipation, respiratory depression, length of ICU and hospital stay, duration of ventilation, hallucinations, delirium, Glascow Coma Scale, endorphins, stress hormones (epinephrine, norepinephrine and/or cortisol), liver function tests and renal function) of the analgesics (morphine and acetaminophen) used for intervention related pain as well as pain titration protocol for pain control in rest.

Study description

Background summary

In 2006, in the Intensive Care Unit (ICU) of the St. Antonius Hospital an analgesia improvement program has been implemented. This program consisted of training of ICU nurses and intensivists using a hospital based standardized pain protocol, and three times daily mandatory measurements of pain levels in rest, rated by the patient himself whenever possible or otherwise by the attending nurse. This program has resulted in a reduction of severe pain levels (NRS>=4) in ICU patients in rest from 41% to 22%. In order to further reduce this percentage, a pain titration protocol is introduced in 2007. As no attention has yet been paid to intervention-related pain levels in these patients, in this prospective study pain control will be studied using different analgesic dosages of morphine around unavoidable painful interventions within a pain titration protocol for pain control in rest.

Study objective

The primary objective of this study is to determine the influence of morphine dosage (2.5 mg vs 7.5 mg) on the percentage of patients with a rated NRS of >= 4 during an painful and unavoidable intervention.

The secondary objectives are to evaluate NRS scores, safety and other aspects of both the intervention related pain protocol (morphine 2.5 mg vs 7.5 mg) as well as the standard pain titration protocol aiming at pain control in rest (paracetamol and morphine), such as nausea, constipation, respiratory depression, length of ICU and hospital stay, duration of ventilation, hallucinations, delirium, Glascow Coma Scale, endorphins, stress hormones (epinephrine, norepinephrine and/or cortisol), liver function tests and renal function. Additionally, a population pharmacokinetic and pharmacodynamic model of morphine and its metabolites will be developed using population pharmacokinetics and/or pharmacodynamics (PK/PD) modelling and covariate analysis in order to develop rational individualized dosing schemes for morphine in ICU patients. Whenever possible the level of sedation or concentration of sedative will be incorporated in the model leading to an analgo-sedative model. Studied covariates will include body weight, age, renal function (ureum, creatinin concentrations and creatinin clearance), liver function, diagnose, Sequential Organ Failure Assessment (SOFA) scores, DNA polymorphisms (μ-opioid receptor, COMT etc) and (perioperative) endorphins and stress hormones (epinephrine, norepinephrine and/or cortisol).

Study design

Prospective, randomized, double blind, clinical trial

Intervention

150 patients will be randomized into two groups, one group will be given 2.5 mg morphine and the other group will be given 7.5 mg morphine, half an hour before the intervention (turning of the patient) Before, during and after the intervention, the patients will be asked to rate the pain using NRS. When the patient is not capable to communicate verbally, the pain ratings are scored by the attending nurse using NRS. For basic pain relief, a standard pain titration protocol is used in all patients, which is current practice in the ICU since 2007.

Study burden and risks

Participation in this study has minimal burden and risks for the patient, as the two different doses of morphine (2.5 and 7.5 mg) administrated before the unavoidable and painful intervention, both are within the therapeutic range. In daily practice doses between 0 to 10 mg morphine are considered to be standard, depending on the attending nurse and physician. Scoring NRS after intervention may be a burden to the patient, because this may lead to a focus of the patient to his pain.
The total amount of blood taken from the patient for this study is 28 ml per day, with an additional 23 ml on the second day of admission to the ICU, and an additional 19.5 ml for patients undergoing cardio- thoracic surgery before

admission to the ICU. These amounts are not expected to influence the recovery of the patient. Moreover, all of the blood samples are taken from an existing arterial line, so no invasive interventions are therefore needed. All the other procedures (NRS scores, Pain titration protocol) are part of the standard care.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients admitted to the ICU of the St. Antonius hospital, with the age of 18 years or older.

Exclusion criteria

- Pregnancy/ breastfeeding
- Language barrier
- Known morphine allergy
- Comatose patient (cooled)
- Patients who are suspected to be braindead
- Unintubated patients on the verge of intubation due to respiratory insufficiency

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2008
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Morphine HCL CF
Generic name:	Morphine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-11-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-12-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-003722-18-NL
CCMO	NL18828.100.07