Effects and adverse events of opioids: a study on the role of pharmacokinetic and pharmacogenetic heterogeneity.

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To study the underlying demographic, clinical and pharmacogenetic factors contributing to the failure of achieving analgesia and/or the occurrence of dose-limiting side effects in individual cancer patients for seperate opioids;- To study if the...

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

Summary

ID

NL-OMON33024

Source
ToetsingOnline

Brief title
Opioids: pharmacokinetics and pharmacogenetics

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer pain, pain in cancer

Health condition

kankerpijn

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMw

Intervention

Keyword: cancer pain, opioids, pharmacogenetics, pharmacokinetics

Outcome measures

Primary outcome

Pain intensity, measured by Numeric Rating Scale

Side effects of opioids: nausea/vomiting, dry mouth, somnolence, obstipation,

myoclonus, confusion, hallucinations, sweating, measured by nurses on a

4-points Likert Scale (none, slight, moderate, severe)

Score on the Delirium Observation Screening Scale (DOS)

Secondary outcome

-

Study description

Background summary

Pain is one of the most frequent symptoms in cancer patients. A majority of these patients need treatment with opioids. In case of moderate-severe pain, strong opioids, step 3 medication from the WHO ladder, are indicated. However, in some patients treated with an opioid of first choice, adequate pain relief without dose-limiting side effects will not be reached. Delirium is one of the most serious side effects. In case of dose-limiting side effects and/or inadequate pain relief, opioid rotation is advised in the Dutch CBO guideline. In case of opioid rotation, the opioid of first choice is changed into another opioid. However, for an individual patient it is not possible to determine which opioid is best for him/her, because the mechanisms underlying the failure of achieving pain relief or the induction of side effects are not known. Treatment, therefore, is based on trial and error. Genetic polymorphism has been suggested to be responsible for the various responses on opioids in

individual patients, either on the level of the metabolism (absorption, distribution, metabolism and axcretion), or on the level of the central nervous system. Scientific reports, however, are scarce and only limited to morphine.

Study objective

To study the underlying demographic, clinical and pharmacogenetic factors contributing to the failure of achieving analgesia and/or the occurrence of dose-limiting side effects in individual cancer patients for seperate opioids;
- To study if the demographic, clinical and pharmacogetic factors contributing to the failure of specific opioids with respect to the achievement of analgesia and/ the occurrence of side effects determine the effect of rotation to another opioid in individual patients;
- To delelop a strategy for opioid rotation with respect to the type of the opioid rotated to and its dose in case of failure on primary treatment with a specific opioid in an individual patient.

Study design

This is a two-year prospective cohort study in which about 1000 cancer patients regularly treated with strong opioids for moderate-severe nociceptive pain will be monitored daily for pain intensity and the occurrence of side effects. In case of dose-limiting side effects and/or inadequate pain relief, opioid rotation will be used; the type of opioid and the route of administration will be choosen according to the clinical situation and the opinion of the responsible caregiver. After infomed consent is given blood will be taken for pharmacogenetic analyses measuring *single nucleotide polymorfisms (SNPs) with possible relevance for the metabolism of opioids and its effects in the central nervous sytem. Patients admitted to the unit for palliative care and symptom control in Erasmus MC Daniel den Hoed Cancer Center will also be asked informed consent to take blood samples for pharmacokinetic analyses of the opioids given. In case of informed consent, blood samples will be taken at specific times during a period of 72 hours after a change in the opioid regimen. The opioids used and their metabolites wil be measured. Opioids and metabolites will also be measured in urine. All clinical and demogaphic data, measurements of pain and side effects and the measurements of SNIP's and pharmacikinetic analyses will be coupled in a database for further analysis of research questions.

Study burden and risks

Patienst will be treated regurarly with strong opioids. Nurse will monitor the effect of the opioids by asking the patients the intensity of pain and side effects. This monitoring also is a standard procedure.
For the study of the pharmacogenetis and pharmacokinetics extra effort is

asked. Blood for pharmacogenetics is taken by a single venapuncture (15 ml). However, for the study of the pharmacokinetics more samples are needed. In that case an intravenous canula will be placed for blood sampling. During 72 hours after a change in the opioid regimen blood samples will be taken twice a day. In case of rescue medication use, 5 extra samples will be taken around the administration of rescue opioid medication. Because the baseline sample then should be taken before the administration of the rescue medication, the delivery of rescue medication may be somewhat postponed.

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

1.Hospitalized cancer patients with moderate or severe nociceptive pain treated with strong opioids.

2. Informed consent.

Exclusion criteria

-

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-01-2010
Enrollment:	1000
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fentanyl medicated plaster, fentanyl citrate
Generic name:	fentanyl
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MS Contin, Oramorph, Morphine hydrochloride
Generic name:	morphine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Oxycontin, Oxynorm
Generic name:	oycodone

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Palladon
Generic name:	hydromorphone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-08-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2009-013022-16-NL
CCMO	NL28399.078.09