Influence of Tapentadol on endogenous modulation of pain in chronic neuropathic pain patients and healthy volunteers

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1. Measure DNIC and offset analgesia in neuropathic pain patients;2. Compare DNIC and offset analgesia in chronic pain patients with DNIC and offset analgesia in healthy volunteers;3. Assess the effect of oral tapentadol on DNIC and offset analgesia...

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

Summary

ID

NL-OMON34371

Source
ToetsingOnline

Brief title
TPT study

Condition

- Other condition

Synonym
pain

Health condition

pijn

Research involving

Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Grunenthal

Intervention

Keyword: endogenous modulation of pain, pain

Outcome measures

Primary outcome

Pain modulation

Secondary outcome

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Study description

Background summary

Endogenous modulation of pain. Pain perception is modulated via facilitatory and inhibitory control systems. Inhibitory control is most important to chronic pain patients as there are strong indications that failed inhibition constitutes a predisposition to acquired chronic pain. Various systems involved in inhibitory control have been demonstrated over the years. Two systems seem important: (1) top-down inhibition of afferent noxious information by endogenous analgesia originating in the periaquaductal grey (PAG) and affecting pain perception via descending pathways; (2) bottom-up activation of pain modulatory systems via activation of spino-bulbo-spinal loops originating in the dorsal horn of the spinal cord. The effect that the latter system has on pain perception is called Diffuse Noxious Inhibitory Control (DNIC). The two systems are interconnected and DNIC is considered a bottom-up activation of the pain modulatory mechanism, as part of the descending endogenous analgesia system. DNIC dysfunctions or is less efficacious in various complex chronic pain states, such as irritable bowel syndrome, chronic headache, fibromyalgia and temporomandibular disorder.

Offset analgesia (OA) is another expression of the endogenous analgesia system and is evoked by noxious stimulation, in order to reduce (or control) the

perception of the noxious event. Offset analgesia becomes apart when an even more painful stimulus occurs briefly during prolonged painful stimulation. Due to activation of the endogenous opioid system the prolonged stimulation is perceived less painful after the intense noxious stimulus than therefore. In a current study (P09.107) we observed that patients with neuropathic pain have a delayed OA or sometimes even absent OA, suggesting a crucial role of pain pathways involved in OA in the development of chronic pain.

Neuropathic pain. Neuropathic pain is a form of chronic pain due to an evident nerve lesion from trauma (incl. surgical trauma), diabetes (small fiber neuropathy), infection (incl. HIV), chemotherapy, etc. The primary sensation is a burning pain coinciding with areas of hyperalgesia and allodynia. In the current study we will focus on patients with chronic neuropathic pain caused by diabetes.

Tapentadol and endogenous modulation of pain. Tapentadol is a centrally acting analgesic with two mechanisms of action: a μ-opioid receptor agonism and noradrenaline (NA) reuptake inhibition. Although the binding of tapentadol to the μ-opioid receptor is weaker than that of morphine its analgesic action is similar to that of morphine due to the (synergistic) effect of the second mechanism (i.e., NA reuptake inhibition). NA plays a role in the endogenous descending pain inhibitory system. Especially at descending pathways NA reuptake inhibition plays a crucial role at the spinal level to reduce chronic neuropathic pain. Hence it is to be expected that tapentadol has a modulatory role on DNIC and OA and consequently will ameliorate pain in chronic neuropathic pain patients.

Study objective

1. Measure DNIC and offset analgesia in neuropathic pain patients;

2. Compare DNIC and offset analgesia in chronic pain patients with DNIC and offset analgesia in healthy volunteers;

3. Assess the effect of oral tapentadol on DNIC and offset analgesia relative to placebo and morphine.

Study design

Randomized double blind

Intervention

Ingestion of pain killer

Study burden and risks

Limited: nausea, sedation, respiratory depression

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

Patient inclusion criteria. (i) Patients diagnosed with small-fiber neuropathy or according to the guidelines of the IASP or other professional pain societies (eg., Netherlands Society of Anesthesiologists); (ii) a pain score of 5 or higher; (iii) age between 18 and 75 years; (iv) being able to give written informed consent.
Volunteer inclusion criteria. Healthy volunteers in the age range 18-75 years of either sex.

Exclusion criteria

Patient and volunteer exclusion criteria. (i) Unable to give written informed consent; (ii) medical disease such as pulmonary, renal, liver, cardiac, gastro-intestinal, vascular (incl. hypertension) disease; (iii) allergy to study medication; (iv) use of strong opioids; (v) use of benzodiazepines; (vi) history of illicit drug abuse or alcohol abuse; (vii) history of psychosis; (viii) epilepsy; (ix) raised intracranial pressure;(x) pregnancy and/or lactation.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	morfine
Generic name:	morfine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tapentadol
Generic name:	Tapentadol

Ethics review

Approved WMO Date:	19-11-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	14-01-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	14-03-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	08-11-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20737
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2010-023175-26-NL
CCMO	NL34186.058.10
OMON	NL-OMON20737