A pilot study on the effect of ARA290 on pain and pain responses and retinal edema in patients with diabetes mellitus and neuropathic pain

Published: 06-07-2010
Last updated: 04-05-2024

To assess the analgesic effect of ARA290 in chronic pain patients

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

Summary

ID

NL-OMON34461

Source
ToetsingOnline

Brief title
ARAP

Condition

- Other condition

Synonym
pain

Health condition

chronische pijn

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: TREND

Intervention

Keyword: chronic pain, neuropathic pain, pain

Outcome measures

Primary outcome

Pain relief

Secondary outcome

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Study description

Background summary

World-wide the development of chronic pain is an extreme burden on patients as well as on society. For example, in the US alone, chronic pain affects more than 70 million Americans (which makes it more widespread than heart disease, cancer and diabetes combined), costing the US economy more than $100 billion per year. Patients with diabetes are particularly prone to develop neuropathic pain. Neuropathic pain is 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 (increased pain sensitivity, i.e., a painful stimulus is perceived more painful) and allodynia (a non-painful stimulus is now perceived as pain). Often (but not always) pain, hyperalgesia and allodynia are restricted to the lower extremities. The neuropathic pain in diabetes ranges from mild to severe, causing the loss of quality of life and inability to participate in the economic work force.

Various treatments have been applied to treat the pain associated with neuropathic pain. Pharmacological treatment varies from the administration of GABA-ergic agents (e.g. Gabapentin) and antidepressants to anesthetics (e.g., ketamine). Most treatments, however, are either ineffective or short-lived. We recently showed that a 4-day treatment with intravenous ketamine is effective in reducing chronic pain from Complex regional Pain Syndrome (type 1) for over

3 months (Sigtermans et al., Pain 2009). Despite the initial effective analgesic effect of ketamine, pain recurred slowly. Hence, repeated treatments are needed. Since this requires repeated multiple-day in-house intravenous infusion therapy this is extremely costly. Taken into account the above we argue that alternative treatments are required, treatments that are effective and do not require multiple-day in-house treatments.

Recently, we assessed the effect of various drugs (ketamine, norketamine, traxoprodil (all NMDA receptor antagonists) and ARA290, an erythropoietin-like drug) on experimentally induced neuropathic pain in the rat. We showed that ARA290 has a beneficial protective effect. Intraperitoneal injections with ARA290 produced a delay in the development of spontaneous pain, allodynia and hyperalgesia following sciatic nerve injury by at least 90 days. In comparison, animals treated with placebo showed immediate pain responses lasting >> 90 days. The ARA290 effect may be explained by assuming that the protein has anti-inflammatory effects at the level of the spinal cord or at supraspinal levels.

ARA290 is an 11-amino acid, linear peptide that is being developed as a tissue protective therapeutic. It mimics the tissue protective pharmacology of erythropoietin (Epo) but is not a hematopoietic stimulant. The ARA 290 peptide has a novel amino acid sequence modeled upon the three-dimensional structure of the region of the Epo molecule that is presumed to bind to and initiate signaling by a tissue protective receptor. This receptor is a heterocomplex of the beta common receptor and the classic erythropoietin receptor (EpoR). Brief interaction of ARA 290 with this receptor results in anti-apoptotic and anti-inflammatory activities in myriad cells, tissues and organs throughout the body including those across tight endothelial barriers such as the blood-brain and blood-retina barrier.

Study objective

To assess the analgesic effect of ARA290 in chronic pain patients

Study design

double-blind, randomized, placebo controlled

Intervention

IV injection with ARA290

Study burden and risks

Liitle to none, excpet the visit to the clinical (3/weeks, 4 weeks)

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

(i) Patients diagnosed with small-fiber neuropathy 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.

Exclusion criteria

Female patients that are pregnant or lactating will be excluded.

Study design

Design

Study phase:	2
Study type:	Interventional
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2010
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ARA290
Generic name:	ARA290

Ethics review

Approved WMO Date:	06-07-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-07-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-11-2011
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2010-021518-45-NL
CCMO	NL33033.058.10