EFFECTS OF TAPENTADOL ON CHRONIC PAIN AND PARAMETERS OF CENTRAL SENSITIZATION. A PROSPECTIVE, OPEN LABEL, RANDOMIZED CROSS-OVER STUDY WITH PREGABALIN AS COMPARATOR,

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48981

Source
ToetsingOnline

Brief title
PRINCE

Condition

- Other condition
- Neurological disorders NEC

Synonym
central sensibilisation, Chronic pain

Health condition

Anesthesiologie, chronische pijn

Research involving
Human

Sponsors and support

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

Intervention

Keyword: chronic pain, chronic sensitization, pregabalin, tapentadol

Outcome measures

Primary outcome

Central Sensitisation parameters

• pressure pain threshold (PPT)

• pressure pain tolerance threshold (PTT)

• conditioned pain modulation (CPM)

• size of allodynia

• Wind-up ratio

• CSI

Secondary outcome

• NRS

• PDI

• PCS

• PVAQ

• Adverse effects of the medications

• Dosages of the medication during the treatment period

Study description

Background summary

Chronic pain is a serious debilitating factor for health and welfare with a mean prevalence of 27% in the general European adult population. In most of these conditions a cause for the pain is seldom to be found. It is speculated that central sensitization (CS) is directly involved in the process of chronification and maintenance of chronic pain in many conditions.
For that reason, alleviation of central sensitization should be part of the treatment of patients with chronic pain. This has been demonstrated for pregabalin, but in case of tapentadol it is unknown if and how it interferes with CS. Most relevant to this study is the association of CS with chronic low back pain, chronic pelvic pain, endometriosis, vulvodynia, and dysmenorrhea as well as interstitial cystitis/bladder pain syndrome.
Tapentadol is a new class of opioids with a dual mechanism of function. Tapentadol agonises the mu-opioid receptor (μ-OR) and inhibits the reuptake of noradrenaline in the central nervous system. Its particular efficacy in managing chronic neuropathic pain that is attributed to the latter mechanism. The noradrenergic effect might result in modulating descending pain pathways in the central neural system and thereby reduce or alleviate CS. Due to the low binding affinity of tapentadol to the μ-OR (with adequate analgesic effects), adverse effects associated with opioid usage such as opioid-induced-hyperalgesia, gastrointestinal complications, dependency and tolerability issues are less likely to occur.
The core of this study is to explore the effects of tapentadol on parameters of CS in patients suffering from chronic pain. This has not been previously performed.

Study objective

The main objective is to determine the change in CS parameters upon administration of tapentadol in comparison to pregabalin in patients suffering from chronic pain that has a visceral or deep somatic origin.

Study design

Prospective, Open-Label, 2X2 Randomized Cross-Over.

Intervention

For tapentadol we will start titrating with 50mg 2x/day and increase the dose

by 50mg 2x/day every 3 days until sufficient analgesia is reached with tolerable adverse effects. The maximum recommended dose is 500 mg per day.

For pregabalin the start dose is 75mg 2x/day. The dose can be increased depending on individual reaction and tolerability of the patient after 3-7 days to reach 150mg 2x/day. If necessary, the dose can be further increased to the maximum dose of 600 mg per day.

Study burden and risks

For the purpose of this study, included patients will be subjected to oral use of Tapentadol and Pregabalin, completing questionnaires and a medication diary and QST assessment.
- Tapentadol and Pregabalin:
o Expected benefits: reducing/alleviating pain.
o Expected risks and burden: insufficient pain reduction, adverse effects and possible carry-over effects during the minimal 2 day washout period.
- Questionnaires
o Expected benefits: insight and more understanding of the nature of pain.
o Expected risks and burden: time investment needed to fill the questionnaires.
- Medication diary
o Patients will keep a daily medical diary, in which they indicate: a painscore, whether they took medication and whether they perceived adverse events of the medication. Furthermore, they can indicate whether additional pain medication was necessary to relief the pain.
- QST
o Expected benefits: deeper insight into the nature of the individual*s pain by testing the presence or absence of CS parameters.
o Expected risks and burden: short lasting pain provocation, time investment and three extra visits to the clinic.

QST and BSE are worldwide applied and considered safe techniques. As one of the applied stimuli measures pain
threshold and pain tolerance, a short-lasting experience of pain might be felt. Risk that a SAE will occur is negligible.

Tapentadol and pregabalin are registered for use in Europe, the extent and nature of their adverse effects are known and both are widely used for neuropathic pain.

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. Gender: female
2. Age: 18 years and older
3. Presence of proven endometriosis or CLBPr
4. Signs of central sensitization
5. No contraindications for opioids or pregabalin.
6. Signed informed consent.

Exclusion criteria

1. No or insufficient understanding of Dutch language.
2. Incapacity to follow instructions.
3. Mental incompetence to provide informed consent.
4. CLBP with radiation to both legs.
5. Pain in one (or more) sites where QST will be applied.
6. Usage of opioids with more powerful spectre, such as oxycodone, fentanyl, morphine in the week prior to start of the study.
7. Previous usage of pregabalin or tapentadol

8. Alcohol abuse.
9. Pregnancy or woman who wish to be pregnant.
10. Kidney and/or liver function disturbances in patients with a medical history (<6 months) of kidney and liverdisturbances

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-03-2019
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lyrica
Generic name:	pregabalin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Palexia
Generic name:	tapentadol
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-07-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2018-001583-34-NL
CCMO	NL65781.056.18