Het effect van opiaten op de werking van bloedplaatjes (P2Y12 receptor remming) bij patiënten met een hartinfarct (ST-Elevation Myocardial Infarction) die vooraf worden behandeld met gemalenTicagrelor

Gepubliceerd: 22-08-2017 Laatst bijgewerkt: 13-12-2022

The hypothesis is that STEMI patients who are pre-treated with crushed ticagrelor and paracetamol have a higher level of platelet inhibition after primary PCI than patients pre-treated with crushed ticagrelor who are treated with fentanyl.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20881

Bron
NTR

Verkorte titel
ON-TIME-3

Aandoening

STEMI
PCI
P2Y12 receptor antagonists
platelet inhibition
Fantanyl
Paracetamol
Ambulance

Ondersteuning

Primaire sponsor: Isala, Zwolle
Overige ondersteuning: AstraZeneca, The Netherlands

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoint of the study is to show that patients with STEMI who are pre-treated with crushed ticagrelor 180 mg and paracetamol 1000 mg have a higher level of platelet inhibition directly after primary PCI compared to patients pre-treated with crushed ticagrelor 180 mg and fentanyl 1-2 mcg/kg with a maximum of 4 mcg/kg. This is measured by the level of platelet reactivity units (PRU) at T2 (directly post-PCI or 1 hour post-angiography.

Toelichting onderzoek

Achtergrond van het onderzoek

Background of the study:

Fast and accurate platelet inhibition is an important therapeutic goal in the acute treatment of patients with ST-segment elevation
myocardial infarction (STEMI). Platelet inhibitory effects induced by normal oral P2Y12 receptor antagonists, for example
ticagrelor, are delayed in STEMI patients undergoing primary percutaneous coronary intervention (primary PCI), which may be
attributed to impaired absorption affecting drug pharmacokinetics (PK) and pharmacodynamics (PD). Another therapeutic goal in
the acute treatment of STEMI is reduction of sympathetic stress and catecholamine release, thereby improving the balance
between the demand for and supply of oxygen, by analgesia like fentanyl of morphine. To date, there are no studies that have
specifically assessed the PD influences of fentanyl on platelet inhibition in STEMI patients who are pre-treated with crushed
ticagrelor tablets. Therefore, In the ON-TIME-3 study, we seek to show the influence of fentanyl on platelet inhibition in STEMI
patients who are pre-treated with crushed ticagrelor in the ambulance.

Objective of the study:

Primary Objective: The aim of the study is to show that STEMI patients who are pre-treated with crushed ticagrelor and
paracetamol have a higher level of platelet inhibition after primary PCI than patients pre-treated with crushed ticagrelor who are
treated with fentanyl.

Study design:

This is a multicenter, prospective, randomized, investigator-initiated open-label study

Study population:

Patients with ongoing chest pain with the diagnosis of STEMI in the ambulance.

Intervention:

Patients are randomized to paracetamol 1000mg iv or fentanyl 1-2 mcg/kg with a maximum of 4 mcg/kg iv.

Primary study parameters/outcome of the study:

The primary endpoint of the study is:

to show that patients with STEMI who are pre-treated with crushed ticagrelor 180 mg and paracetamol 1000 mg have a higher
level of platelet inhibition directly after primary PCI compared to patients pre-treated with crushed ticagrelor 180 mg and fentanyl
1-2 mcg/kg with a maximum of 4 mcg/kg.

Doel van het onderzoek

The hypothesis is that STEMI patients who are pre-treated with crushed ticagrelor and paracetamol have a higher level of platelet inhibition after primary PCI than patients pre-treated with crushed ticagrelor who are treated with fentanyl.

Onderzoeksopzet

Blood sample measurements for platelet function testing and level of active metabolite of ticagrelor, using Verify Now P2Y12 assay (Accumetrics, San Diego, California), will be done at four time points:

- 1: when arriving at the cathlab

- 2: directly post-primary PCI or 1 hour after coronary angiography when no PCI was performed

- 3: one hour post-primary PCI including electrocardiogram (ECG) or 2 hours post- coronary angiography

- 4: six hours post-primary PCI of 7 hours post-coronary angiography

Onderzoeksproduct en/of interventie

Patients are randomized to paracetamol 1000 mg iv or fentanyl 1-2 mcg/kg with a maximum of 4 mcg/kg iv.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. age >17 years

2. referred by ambulance paramedics to Isala (Zwolle) or Zuyderland Hospital (Heerlen)

3. diagnosed in the ambulance with STEMI defined as:

- ongoing chest pain >30 minutes and <12 hours duration and

- ST-segment elevation >0.1 mV in at least 2 contiguous leads

4. ongoing chest pain with a pain score (NRS) ¡Ý4

5. the patient has been informed of the nature of the study, agrees to its provisions and has provided verbal informed consent in the pre-hospital phase followed by written informed consent in hospital

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. presenting with cardiogenic shock; defined as:

- systolic blood pressure <90 mmHg and

- heart rate >100/min and

- peripheral oxygen saturation <90% (without oxygen administration)

2. patients with a nasogastric tube in situ or requiring a nasogastric tube

3. patients who already received fentanyl or paracetamol <2 hours prior to randomization

4. patients on current treatment with P2Y12 inhibitors
(ticagrelor, clopidogrel or prasugrel)

5. allergy to morphine or paracetamol

6. patients with recent major bleeding complications or contraindication to dual antiplatelet therapy:

- hypersensitivity to aspirin or ticagrelor

- current use of (new) oral anticoagulation

- history of bleeding diathesis or known coagulopathy

- refusal of blood transfusions

- history of intracerebral mass, aneurysm, arteriovenous malformation, or hemorrhagic stroke

- known severe liver dysfunction

7. received any organ transplant or is on a waiting list for any organ transplant

8. patients undergoing dialysis

9. pregnant or lactating female

10. patients currently participating in another investigational drug or device study

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-12-2017
Aantal proefpersonen:	190
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	22-08-2017
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6603

Register	ID
NTR-old	NTR6785
Ander register	: (CCMO) ABR 62462 NL62462.075.17

Resultaten