TAME Cardiac Arrest Trial. Targeted Therapeutic Mild Hypercapnia After Resuscitated Cardiac Arrest: A Phase III Multi-Centre Randomised Controlled Trial

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The primary objective of this study is to determine whether targeted therapeutic mild hypercapnia (TTMH) improves neurological outcome at 6 months compared to standard care (targeted normocapnia) (TN).

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

Summary

ID

NL-OMON46761

Source
ToetsingOnline

Brief title
TAME

Condition

- Cardiac arrhythmias
- Encephalopathies

Synonym
Postanoxic encephalopathy; brain injury after cardiac arest

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Project Grant from the Australian National Health and Medical Research Council (NHMRC) Project Grant ID APP1119855; and;a Definitive Interventions and Feasibility Awards 2017 (Project Grant ID DIFA-2017-036) 2017 by the Irish Health Research Board (HRB).

Intervention

Keyword: Cardiac Arrest, cardiopulmonary resuscitation, hypercapnia

Outcome measures

Primary outcome

The primary outcome measure for this study is the proportion of patients with a favourable neurological outcome at 6 months as assessed using the GOSE.

Secondary outcome

(I) Mortality at ICU and hospital discharge and at 6 months after randomisation.

(II) Functional recovery as measured by the proportion of patients with a favourable functional outcome at 6 months after randomisation as assessed using the modified Rankin scale and the Cerebral Performance Category

(III) Cognitive functional recovery assessed at 6 months after randomisation using the Montreal Cognitive Assessment; Informant Questionnaire on Cognitive Decline; Symbol Digit Modalities Test and 30-second chair test.

(IV) Quality of life at 6 months after randomisation assessed by the five domains of Mobility, Self-care, Usual Activity, Pain/discomfort, and Anxiety/Depression of the EQ-5D-5L scale.

(V) Safety as determined as the proportion of adverse events occurring between groups as reported by treating clinicians.

(VI) A health economic assessment will be performed to evaluate differences in

costs for hospital length of stay and destination at discharge for patients

allocated to TTMH and standard care (TN).

Study description

Background summary

Cardiac arrest is a common and catastrophic event. Out-of-hospital cardiac arrest has an estimated incidence of approximately 1 per 1,000 persons per year with mortality rates varying between 87 to 94%. Once admitted to an Intensive Care Unit (ICU), survival is still unacceptably low at approximately 40% and has remained unchanged over the last decade. These ICU mortality is mainly due to severe cerebral injury sustained during CPR and after return of circulation (reperfusion injury). Accordingly, while the initial problem is cardiac in nature, after ICU admission, the dominant reason for such dismal outcomes is neurological injury. Thus, a better neurological outcome is the logical and dominant therapeutic goal in a population where more than half are of working age. The brain is particularly susceptible to damage following return of spontaneous circulation with reperfusion injury and inflammation both of which may contribute to subsequently increased vascular resistance and sustained hypoperfusion. PaCO2 is the major determinant of cerebral blood flow in man. The in this study proposed therapeutic CO2 target was simple, easy to aim for, with no signs of harm and cost free. Together with the large epidemiological study, double crossover physiological study and phase II trial already conducted, there is now epidemiological, biological, physiological, and supportive clinical data suggesting that TTMH can deliver significant outcome improvements in resuscitated cardiac arrest patients admitted to ICU. These findings strengthen the need to perform a larger phase III trial to address the question of whether targeting mild therapeutic hypercapnia improves patient-centred outcomes in resuscitated cardiac arrest patients admitted to the ICU. Thus, a larger definitive phase III trial is needed now.

Study objective

The primary objective of this study is to determine whether targeted therapeutic mild hypercapnia (TTMH) improves neurological outcome at 6 months compared to standard care (targeted normocapnia) (TN).

Study design

This a phase III multi-centre, randomised, parallel-group, controlled trial in

resuscitated cardiac arrest patients who are admitted to the intensive care unit.

Intervention

targeted therapeutic mild hypercapnia (TTHM) aiming at a PaCO2 of 50-55 mmHg during 24 hours versus standard care

Study burden and risks

Burden and risks associated with participation in this study are very small. Patients randomized to the intervention arm might have a benefit of the treatment.

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. Adult (age *18 years or older)
2. Out-of-hospital cardiac arrest of a presumed cardiac or unknown cause
3. Sustained ROSC * defined as 20 minutes with signs of circulation without the need for chest compressions
4. Unconscious (FOUR-score motor response of <4, not able to obey verbal commands after sustained ROSC)
5. Eligible for intensive care without restrictions or limitations
6. Within <180 minutes of ROSC

Exclusion criteria

1. Unwitnessed cardiac arrest with an initial rhythm of asystole
2. Temperature on admission <30 C
3. On ECMO prior to ROSC
4. Obvious or suspected pregnancy
5. Intracranial bleeding
6. Severe chronic obstructive pulmonary disorder (COPD) with long-term home oxygen therapy

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-09-2019

Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	28-02-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
ClinicalTrials.gov	NCT03114033
CCMO	NL62674.018.17