Efficacy and safety of home treatment versus in hospital treatment with LMWH in patients with non-massive pulmonary embolism

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1. To evaluate the efficacy and safety of out of hospital treatment with LMWH and Vitamin K antagonists in consecutive patients with objectively proven acute non-massive pulmonary embolism2. To perform a health economics evaluation in all patients3...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Pulmonary vascular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON32323

Source
ToetsingOnline

Brief title
The Hestia Study

Condition

- Pulmonary vascular disorders

Synonym
Pulmonary embolism, Venous-thromboembolism

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline

Source(s) of monetary or material Support: onafhankelijke onderzoekersbeurs

Intervention

Keyword: Home treatment, Low-molecular-weight-heparin, Pulmonary embolism

Outcome measures

Primary outcome

1. Recurrent thromboembolic events are defined as recurrent pulmonary embolism if demonstrated by new defects on helical CT scan, perfusion-ventilation lung scan or pulmonary angiography or PE at autopsy or a clinical report indicating PE as the (likely) cause of death; or deep vein thrombosis demonstrated by compression ultrasonography or contrast venography.

2. Bleeding is defined as major if it is clinically overt e.g. a clinically apparent bleeding or sign and symptoms suggestive of bleeding confirmed with imaging studies (ultrasound, computer tomography (CT)) combined with at least one of the following situations:

a) Critical site involvement e.g. intracranial, retroperitoneal, intraocular, intraspinal, pericardial or non-traumatic intra-articular.

b) Bleeding associated with a decrease in hemoglobin level of 1.3 mmol/L (2.0 gr/dl) or more.

c) Bleeding leading to transfusion of > 2 units of whole blood or packed red cells.

d) Fatal bleeding.

3. The cause of death in patients who die within the study period of six months is assessed by autopsy or a clinical report indicating the - likely - cause of

death.

Secondary outcome

- a health economics evaluation in all patients

- a quality of life evaluation in all patients

Study description

Background summary

Acute pulmonary embolism (PE) continues to cause morbidity and mortality and contributes to up to 200.000 deaths annually in the United States. Intravenous unfractionated heparin (UFH), given as inpatient treatment, followed by vitamin K antagonists for a period of six months, has been the part of standard treatment of venous thromboembolism for several years. Several clinical trials have demonstrated that administration of low molecular weight heparin (LMWH) once or twice daily is at least as effective as UFH in preventing recurrent venous thromboembolism (VTE) with comparable safety regarding the occurrence of major haemorrhages. LMWH's have a number of advantages over the standard UFH. They can be administered subcutaneously, have a more predictable anticoagulant response, which renders laboratory control unnecessary, and make home treatment in patients with VTE potentially feasible. The results of randomised studies have demonstrated that LMWH is also as effective as UFH in the treatment of patients with symptomatic acute non-massive PE.
Among patients with PE, there is a group of patients, which is at low risk for adverse events and thus may be potentially amenable to outpatient management. Once this low risk group is identified, a less complex and less resource-intensive but equally efficacious and safe treatment is warranted, allowing for earlier discharge or even prevent hospitalisation. Although LWMH has been widely used for treatment of deep venous thrombosis (DVT) out of hospital, their use for out of hospital treatment in patients with acute PE has not been widely studied.
Two prospective cohort studies have been carried out to evaluate the feasibility of home treatment for acute PE. In the first study, performed in 108 patients, outpatient treatment with LMWH in patients with PE led to recurrent VTE and major bleeding in 5.6 % and 2.0 % of patients, respectively, and with rather wide confidence limits around these incidences. Strength of this study is that a simple triage model to assess eligibility for home treatment was used. In the second study, a study nurse treated 70 patients at home. In one patient a recurrent PE occurred (1.4 %) while another patient got haemoptysis (1.4%). Finally, in a recent study patients presenting with acute

DVT and/or acute PE were randomised to treatment with either Tinzaparin or Dalteparin once-daily after which vitamin K antagonists (VKA) was continued for a period of at least three months on an outpatient basis. In this study a straightforward triage protocol was used to exclude patients with a too high risk for outpatient treatment. Of the 505 patients randomised only 90 had acute PE. The composite endpoint of recurrent VTE and major bleeding was not different between the two treatment groups, being 4.4 % and 5.9 % in the Dalteparin and Tinzaparin group respectively (p=0.44). Among the PE patients, only 2 had a recurrent VTE event (1 DVT, 1 PE) while major haemorrhage did not occur.

In conclusion, while evidence is accumulating that initial home treatment of patients with acute PE may be feasible and safe, no study has conclusively demonstrated effective and safe out of hospital treatment in patients with acute PE. Given this limited evidence, clinicians remain reluctant to routinely treat patients with non-massive pulmonary embolism at home with LMWH and as a result, nearly all patients presenting with acute PE still receive initial treatment at the hospital.

Study objective

1. To evaluate the efficacy and safety of out of hospital treatment with LMWH and Vitamin K antagonists in consecutive patients with objectively proven acute non-massive pulmonary embolism
2. To perform a health economics evaluation in all patients
3. To perform a quality of life evaluation in all patients.

Study design

Triage based cohort follow-up study in patients with acute PE treated out of hospital

Study burden and risks

Benefit: Patient satisfaction may be higher in home treatment.

Risk: late complications of PE or bleeding can not managed as quick and effective in a home setting as in a hospital setting

Contacts

Public
GSK

v Deventerln 20
3528AE Utrecht
Nederland
Scientific
GSK

v Deventerln 20
3528AE Utrecht
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Consecutive patients with proven acute non-massive, stable PE
2. Age over 18
3. Informed consent

Exclusion criteria

1. Patients who have had symptoms of PE for longer than 7 days duration
2. Diagnosis of PE during anticoagulant treatment
3. Active bleeding, or a very high risk for major bleeding
4. Severe pain requiring intravenous narcotic analgesia
5. Medical or social condition which necessitates admission to the hospital for another reason
6. Pregnancy
7. Severe renal of liver failure
8. Previously documented heparin induced thrombocytopenia

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2009
Enrollment:	280
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
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
CCMO	NL20837.058.07