PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Long term anticoagulation with low-molecular-weight heparin in a cohort of early neurological rehabilitation patients: does an effective inhibition of activity of factor Xa and factor IIa occur, as well as an increase of tPA and TFPI-levels?

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

In early neurological rehabilitation patients, partly treated with low-molecular-weight heparins for longer periods due to prophylactic or therapeutic causes, coagulation parameters as well as biological markers of the heparin effect should be evaluated 7 days after treatment initiation as well as over a longer time period.

Brief Summary in Scientific Language

In early neurological rehabilitation units, patients after embolic stroke, intracranial bleeding, subarachnoid hemorrhage, craniocerebral injury, cerebral hypoxia, critical illness polyneuropathy and further neurological/neurosurgical diseases are treated. If indicated (e.g. in case of atrial fibrillation, after heart valve replacement or thrombosis/pulmonary embolism), low molecular weight heparins are administered in therapeutic dosages. Other patients in early neurological rehabilitation are treated with low molecular weight heparins due to thrombosis prophylaxis. A monitoring of LMWH-therapy is currently only recommended for several LMWHs in case of renal function impairment. In this observational design study, it should be demonstrated in a cohort of long term treated patients of early neurological rehabilitation, in which extend activity of FXa and FIIa are inhibited by the in this clinic solely used LMWHs tinzaparin and enoxaparin. In addition, it should be evaluated, whether levels of the biological marker of the heparin effect, TFPI, are increased. Moreover, D-Dimer levels as marker for unapparent thrombotic events will be analyzed as well as the endogenous thrombin potential (ETP). Comparable investigations are presently not existent. This investigation should contribute to the evaluation of a potential relevancy of a monitoring of LMWH therapy in this risk collective.

Organizational Data

- DRKS-ID: **DRKS00000083**
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DRKS-ID: **DRKS00000083**
Date of Registration in DRKS: **2009/03/19**

- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **Geschäfts-Nr.: 251/07 , Ethikkommission des Fachbereichs Humanmedizin der Johann-Wolfgang-Goethe-Universität Frankfurt am Main**

Secondary IDs

Health condition or Problem studied

- Free text: **prophylactic LMWH-administration due to temporary or lingering patient's immobility due to their neurological/neurosurgical disease (cohorts 3+4)**
- Free text: **therapeutic LMWH-administration due to atrial fibrillation, thrombotic or thrombembolic events (cohorts 1+2).**
- Free text: **administration of oral anticoagulants due to atrial fibrillation, thrombotic or thrombembolic events (cohort 5, control cohort)**
- ICD10: **I74 - Arterial embolism and thrombosis**
- ICD10: **I48.1 - [generalization I48: Atrial fibrillation and flutter]**

Interventions/Observational Groups

- Arm 1: **Blood withdrawals for determination of coagulation parameters on an observational cohort of early neurological rehabilitation patients under therapeutic tinzaparin treatment (90 IE anti-Xa/kg BID subcutaneously). Samplings take place on day 7 as well as one month and two months after treatment initiation with therapeutic tinzaparin. Samples are withdrawn on these days before Tinzaparin-administration ("0h", minimum level) as well as 4h ("4h", peak level) and 12 h thereafter, before second LMWH-administration on that day. Tinzaparin treatment by itself displays no intervention, solely the samplings for coagulation parameter determination do.**
- Arm 2: **Blood withdrawals for determination of coagulation parameters on an observational cohort of early neurological rehabilitation patients under therapeutic enoxaparin treatment (100 IE anti-Xa/kg BID subcutaneously). Samplings take place on day 7 as well as one month and two months after treatment initiation with therapeutic enoxaparin. Samples are withdrawn on these days before enoxaparin-administration ("0h", minimum level) as well as 4h ("4h", peak level) and 12 h thereafter, before second LMWH-administration on that day. Enoxaparin treatment by itself displays no intervention, solely the**

samplings for coagulation parameter determination do.

- Arm 3: **Blood withdrawals for determination of coagulation parameters on an observational cohort of early neurological rehabilitation patients under prophylactic tinzaparin treatment (4500 IE anti-Xa OD subcutaneously). Samplings take place on day 7 as well as one month and two months after treatment initiation with prophylactic tinzaparin. Samples are withdrawn on these days before Tinzaparin-administration ("0h", minimum level) as well as 4h ("4h", peak level) thereafter. Tinzaparin treatment by itself displays no intervention, solely the samplings for coagulation parameter determination do.**
- Arm 4: **Blood withdrawals for determination of coagulation parameters on an observational cohort of early neurological rehabilitation patients under prophylactic enoxaparin treatment (4000 IE anti-Xa OD subcutaneously). Samplings take place on day 7 as well as one month and two months after treatment initiation with prophylactic enoxaparin. Samples are withdrawn on these days before enoxaparin-administration ("0h", minimum level) as well as 4h ("4h", peak level) thereafter. Enoxaparin treatment by itself displays no intervention, solely the samplings for coagulation parameter determination do.**
- Arm 5: <style fontName='DejaVu Sans' isBold='true'>Blood withdrawals for determination of coagulation parameters on an observational cohort of early neurological rehabilitation patients under treatment with oral anticoagulants (control cohort). Samplings take place on tweo days, separeted by 4 weeks, at corresponding timepoints ("0h" & "4h"), as in cohorts 3 and 4. Oral anticoagulant treatment by itself displays no intervention, solely the samplings for coagulation parameter determination do.</style>

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **Non-randomized controlled trial**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Other**
- Assignment: **Other**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

anti-FXa-activity - measured on an ACL6000 coagulation analyzer

samplings take place on day 7 as well as one month and two months after treatment initiation with LMWH. Anti-FXa-activity is analyzed on these days before LMWH-administration ("0h", minimum level) as well as 4h ("4h", peak level) and - in case of therapeutic indication/dosage treated patients - 12 h thereafter, before second LMWH-administration on that day . In control cohort patients, (cohort 5, oral anticoagulants), samplings take place at corresponding timepoints ("0h" & "4h") at 2 different occasions, separated by 4 weeks.

Secondary Outcome

anti-FIIa-activity - measured on an ACL6000 coagulation analyzer.

plasma levels of D-Dimer and TFPI - measured by ELISA technique.

endogenous thrombin potential (ETP) - measured on a Fluoroskan Ascent Type 374 microplate fluorometer.

samplings take place on day 7 as well as one month and two months after treatment initiation with LMWH. Anti-FIIa-activity as well as the further secondary endpoint parameters are analyzed on these days before LMWH-administration ("0h", minimum level) as well as 4h ("4h", peak level) and - in case of therapeutic indication/dosage treated patients - 12 h thereafter, before second LMWH-administration on that day . In control cohort patients, (cohort 5, oral anticoagulants), samplings take place at corresponding timepoints ("0h" & "4h") at 2 different occasions, separated by 4 weeks.

D-Dimer-levels will be analyzed only of "0h"-samples.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2007/11/08**
- Target Sample Size: **90**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

patients of early neurological rehabilitation under therapeutic or prophylactic LMWH treatment

patients of early neurological rehabilitation under oral anticoagulant treatment

Exclusion criteria

necessity of periodical hemodialysis treatment.

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

- **Institutional budget , no external funding (budget of sponsor/PI)**

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Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2008/10/31**

Trial Publications, Results and other documents

- Paper **[---]***
- Abstract **[---]***

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*