A Double-Blind clinical trial of Benfotiamine Treatment in Diabetic Nephropathy

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-To investigate whether a short-term treatment (3 months) with benfotiamine in diabetic nephropathy patients leads to a reduction in urinary excretion of β2-microglobulin and albumin.-To investigate whether short-term treatment (3 months)...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON31030

Source
ToetsingOnline

Brief title
Benfotiamine in Diabetic Nephropathy

Condition

- Diabetic complications
- Nephropathies

Synonym
diabetes with kidney complications

Research involving
Human

Sponsors and support

Primary sponsor: Isala Klinieken
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: benfotiamine, diabetes, nephropathy

Outcome measures

Primary outcome

Change in urinary excretion of: (measured in 24-hour urine)

• β2-microglobulin

• Albumin

Secondary outcome

Change in urinary excretion of: (measured in 24-hour urine)

• KIM-1 (kidney injury molecule-1)

• MIF (macrophage inhibiting factor)

• MCP-1 (monocyte chemo-attractant protein-1)

• C3d

• Urinary peptidomics

• Reactive oxygen species, advanced glycation end-products (AGEs), and

carbonylated albumin

Study description

Background summary

Diabetic nephropathy is a serious complication of diabetes mellitus, which is the leading cause of end-stage renal disease (ESRD) in the Western World. Benfotiamine has been shown to reduce diabetic nephropathy and retinopathy in animal experimental models. We will investigate the effect of benfotiamine supplementation in patients with diabetic nephropathy, and hypothesize that it will slow down the progression to ESRD if it leads to reduction of tubulointerstitial damage and inflammation.

Study objective

-To investigate whether a short-term treatment (3 months) with benfotiamine in diabetic nephropathy patients leads to a reduction in urinary excretion of β2-microglobulin and albumin.
-To investigate whether short-term treatment (3 months) with benfotiamine in diabetic nephropathy patient leads to a reduction in urinary excretion of markers of renal tubulointerstitial damage (Kidney Injury Molecule 1, Monocyte Chemoattractant Protein 1, Macrophage Inhibiting Factor, Complement factor C3d)

Study design

Mono-center, randomized, controlled, double-blind, parallel clinical trial studying the effect of high dose benfotiamine compared to placebo in 66 patients with diabetic nephropathy. The study consists of two phases:
1- Run-in phase (6 weeks): In this phase patients will be instructed on collection of 24h urine samples, it will be checked whether they have urinary albumin excretion consistently in the microalbuminuric range, and they will be instructed on maintenance of stable diet and activity levels prior to the study visits to the outpatient clinic.
2- Treatment phase 1 (12 weeks): In random order, benfotiamine is given to one half of the patients and placebo is given to the other half.

Intervention

-Treatment phase 1 (12 weeks):
Group A: Benfotiamine (300 mg) 3x 1 film coated tablet daily (900 mg daily dose benfotiamine)
Group B: Placebo 3x 1 film coated tablet daily

Study burden and risks

-The patients are asked to attend the outpatient clinic for the study 6 times in total. Before each visit the patients are asked to collect a 24h urine sample. They will be asked to refrain from food from the previous evening to take fasting blood samples (5 vials of 7 ml). In addition, a second-morning urine sample will be collected.
-No other physical or physiological discomfort in association with participation is anticipated than the discomfort associated with the collection of the 24h urine samples and the blood sampling. There are no known risks associated with the investigational product other than the rare occurrence of urticaria and pruritus.
-Benfotiamine will be investigated to assess its effect on markers of tubulointerstitial damage and inflammation associated with diabetic nephropathy. If it will be demonstrated that benfotiamine causes an improvement in these markers, the drug may become eligible for further large studies on its

efficacy in prevention of the development of end-stage renal disease in susceptible diabetic patients. Participation of diabetic nephropathy patients in this study is of great importance, and answering the questions of this clinical trial is not possible without observing and analyzing the parameters at the end of the study.

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

• Diabetes mellitus, with onset of disease after the age of 40 years
• Age: 50-70 years
• Patients are on treatment with angiotensin converting enzyme inhibitors (ACEi) and/or angiotension II antagonists (AIIA) in an unchanged dose for at least 3 months
• Active diabetic nephropathy as indicated by presence of microalbuminuria (30-300 mg/24 h

urine) in at least two samples within 2-6 weeks in advance of inclusion in the trial
• HbA1c < 8.5%, a higher HbA1c < 9.5% is acceptable if the treating phycisian and the patient have accepted that striving for lower values is an unreachable goal (patients with high HbA1c values are the ones that one would expect to be benefit most from treatment with benfotiamine)
• eGFR (estimated by MDRD formula) > 30 ml/min
• Males and postmenopausal females
• Written informed consent

Exclusion criteria

• Renal impairment by other causes than diabetes
• Stage of the disease more severe than indicated in "Inclusion criteria" (macroalbuminuria or renal insufficiency)
• Severe hypoglycemia during the last 3 months, needing help from another person
• Severe hepatopathy (laboratory values about three times higher than normal)
• Endocrine disorders, e.g. hyper-/hypothyroidism
• Blood pressure > 160/90 mmHg
• Severe cardiac function disturbances and severe heart rhythm disturbances
• Neoplasms
• Severe general diseases or mental disorders making the participation in the study impossible
• Drug abuse
• Female patients during pregnancy and lactation period and female patients with active menses during the past year
• Hypersensitivity to benfotiamine or other constituents of the study medication
• HbA1c >9.5%
• Use of vitamin B containing supplements during the last 3 months
• Use of NSAIDs more than 3 times per week (including self-medication)
• Participation in another study within one month before entering the benfotiamine study

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-03-2008
Enrollment:	86
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Milgamma mono
Generic name:	Benfotiamine

Ethics review

Approved WMO Date:	30-10-2007
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	15-11-2007
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2007-001755-19-NL
CCMO	NL17390.075.07